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(54) **6,9-DISUBSTITUTED PURINE DERIVATIVES AND THEIR USE AS COSMETICS AND COSMETIC COMPOSITIONS**

6,9-DISUBSTITUIERTE PURINDERIVATE UND IHRE VERWENDUNG ALS KOSMETIKA UND KOSMETISCHE ZUSAMMENSETZUNGEN

DÉRIVÉS DE PURINE 6,9-DISUBSTITUÉE ET LEUR UTILISATION EN TANT QUE PRODUITS COSMÉTIQUES ET COMPOSITIONS COSMÉTIQUES

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- **ZHANG R ET AL: "CYTOKININ BIOCHEMISTRY IN RELATION TO LEAF SENESCENCE III. THE SENESCENCE-RETARDING ACTIVITY AND METABOLISM OF 9-SUBSTITUTED 6 BENZYLAMINOPURINES IN SOYBEAN LEAVES", JOURNAL OF PLANT GROWTH REGULATION, SPRINGER VERLAG, NEW YORK, NY, US, vol. 8, no. 3, 1 January 1989 (1989-01-01) , pages 181-198, XP008128462, ISSN: 0721-7595**
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EP 2 245 031 B1

Description

Technical Field

[0001] The invention relates to 6,9-disubstituted purine derivatives as well as their use as, or in, cosmetics and/or cosmetic preparations.

Background Art

[0002] In recent years, 6-substituted aminopurines have assumed considerate biochemical significance. Some compounds of this type promote plant growth and belong to the group of growth regulators termed cytokinins (Letham, Ann. Rev. Plant. Physiol. 18,349,1967). In cytokinin bioassays based on induction of cell division in plant tissue cultures, the most active compound is the naturally occurring cytokinin *trans*-zeatin (6-((E)-4-hydroxy-3-methylbut-2-enylamino)purine: Letham, Planta 74:228,1967). Cytokinins closely related to zeatin occur as bases in soluble RNA (Skoog et al., Science 154:1354, 1966). In the serine and tyrosine RNAs of yeast, plants, and animals the cytokinin is adjacent to the anticodon. The growth of mammalian cell cultures is inhibited by certain N^6-substituted adenosines with cytokinin activity (Grace et al., Proc.Am.Assoc.Cancer Res. 8:23, 1967). After the discovery of kinetin (Miller et al., J.Amer.Chem.Soc. 77:1392,1955), there was a flurry of activity that led to the finding of 6-benzylaminopurine (BA), an active and easily obtainable cytokinin. Much research into cytokinin physiology was subsequently done with this substance.

[0003] Alkylation of natural cytokinins at position 9 of the purine nucleus may occur in plants. Lupinic acid, a zeatin conjugated at N9 with the amino acid alanine, was the first detected metabolite of this type (MacLeod et al., J.Org.Chem. 41: 3959, 1976; Duke et al., Phytochemistry 18:819, 1978; Parker et al., Planta 142:239, 1978). Later, the corresponding 9-alanyl derivative was identified as a metabolite of BA in bean seedlings (Letham et al., Phytochemistry 17:2053, 1979; Zhang et al., J. Plant Growth Regul. 8:181, 1989). Like 9-alanyl zeatin, it exhibited low biological activity and higher stability than the corresponding bases (Parker et al., Planta 142:239, 1978; Palni et al., Planta 160:242, 1984; Zhang et al., J. Plant Growth Regul. 8:181, 1989). The minimisation of BA conjugation has been of both biotechnological and agronomic interest for some time (see, e.g., Zhang et al., J. Plant Growth Regul. 8:181, 1989; Werbrouck et al., Physiol. Plant. 98:291, 1996). 9-Substituted BA derivatives which slowly release free BA may possess enhanced cytokinin activities (e.g., senescence retarding, *in vitro* morphogenesis, cell division stimulating, etc.) since these compounds are not directly subject to inactivation by conjugation.

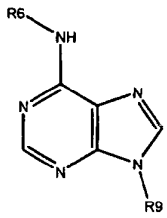
[0004] A number of 9-substituted cytokinin derivatives have been reported but their structure activity relationships still remain an enigma. The most effective 9-alkyl derivatives developed so far are 9-(2-tetrahydropyranyl)-BA (van Overbeek et al., Science 156:1497,1967) and 9-(2-tetrahydrofuranyl)-BA (Zhang et al., J. Plant Growth Regul. 8:181, 1989), which both proved to be considerably more active than BA in evoking several growth responses. Since the tetrahydropyranyl group is readily cleaved by acid hydrolysis, it had been suggested that the high biological activity of 9-(2-tetrahydropyranyl)-N^6-alkyladenines is probably a consequence of slow cleavage of the 9-substituent (Young et al., Phytochemistry 8: 1199, 1969). Subsequently, Fox et al. (Plant Physiol. 47:275, 1971) studied the metabolism of the less active 9-methyl-BA in tobacco and soybean callus tissue and demonstrated rapid conversion to several products. The metabolites were not identified definitively, although it was proposed that conversion to free BA occurred. Pietraface et al., (Physiol. Plant. 53:249, 1981) examined the metabolism of 9-methyl-BA in germinating lettuce seed and suggested formation of BAR and BAR5'P on the basis of chromatographic data. Nevertheless, free BA was not detected. Finally, the application of a 9-(2-tetrahydropyranyl)- and a 9-(2-tetrahydrofuranyl)-BA, assessed for their ability to retard soybean leaf senescence, led to release of free BA (Zhang et al., J. Plant Growth Regul. 8:181, 1989). Both compounds were also debenzylated to adenine substituted with 9-tetrahydropyranyl and 9-tetrahydrofuranyl moiety, respectively. The observed high activity of these 6-benzylamino-9-alkylpurines could be a consequence of their ability to release the free base and to maintain an optimal concentration of the free base concentrations over a prolonged period (Zhang et al., J. Plant Growth Regul. 8:181, 1989). Thus, the susceptibility to enzymatic dealkylation is probably the critical factor determining the biological activity of 9-alkyl cytokinins. Hence the less active compounds (Kende et al., Plant Physiol. 43: 1244, 1968; Young et al., Phytochemistry 8:1199, 1969; Corse et al., J. Plant Growth Reg. 8:211, 1989; Motyka et al., SPB Acad Publ., ISBN 90-5103-066-5, p. 215, 1992) are probably not susceptible to cleavage of the 9-substituent and exhibit low or zero activity because of their stability. The enhanced activity of 9-alkyl-BAs relative to those of BA, can be consequently attributed to their ability to gradually release the active free base.

[0005] US 2007/009474 discloses n-benzyl-9-(2-tetrahydropyranyl)adenine for treating skin.

[0006] This invention provides growth-regulatory, differentiating, and antisenescent cytokinin analogues having improved selectivity and efficiency index (i.e., that are less toxic yet more efficacious) than analogues known heretofore.

Disclosure of the invention

[0007] This invention provides 6,9-disubstituted purine derivatives of the general formula I



I

and their pharmaceutically acceptable salts

wherein R6 is an alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycle, heterocycloalkyl, heteroalkyl, or arylalkyl group containing at least one hydroxyl substitution thereon, and
wherein R9 is a tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, or 1-ethoxyethyl group;
wherein alkyl denotes a branched or unbranched alkyl chain containing 1 to 8 carbon atoms, which is optionally substituted independently with 1 to 7 substituents selected from the group containing hydroxyl, halogen, alkyloxy, aryloxy, alkylamino, arylamino, amino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, alkyloxycarbonylamino, aryloxycarbonylamino, aryl, heterocycle and heteroaryl group;
wherein alkenyl denotes a branched or unbranched alkenyl chain containing 2 to 7 carbon atoms with at least one double bond therein (e.g., vinyl, allyl, 1-propenyl, 1-methylethenyl, but-1 to 3-enyl, pent-1 to 4-enyl, hex-1 to 5-enyl, hept-1 to 6-enyl, allyl, isopentenyl, dimethylallyl) being optionally substituted independently with 1 to 6 substituents selected from the group containing halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group,
wherein alkynyl denotes a branched or unbranched alkynyl chain containing 2 to 7 carbon atoms with at least one triple bond therein (e.g., ethynyl, propargyl, methylethynyl, but-1 to 3-ynyl, pent-1 to 4-ynyl, hex-1 to 5-ynyl, hept-1 to 6-ynyl) being optionally substituted Independently with 1 to 6 substituents selected from the group containing halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, alkyloxycarbonylamino, and aryloxycarbonylamino group;
wherein cycloalkyl denotes a monocyclic or polycyclic alkyl group containing 3 to 15 carbon atoms (e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or adamantyl) being optionally substituted independently with 1 to 7 substituents selected from the group containing halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein aryl denotes an aromatic carbocyclic group containing 6 to 18 carbon atoms with at least one aromatic ring or a multiple condensed ring with at least one aromatic ring (e.g., phenyl, biphenyl, naphthyl, tetrahydronaphtyl, fluorenyl, indenyl, phenanthrenyl, 1,2,3,4-tetrahydronaphtyl, naphtyl, anthryl, or phenantryl), which is optionally substituted independently with 1 to 7 substituents selected from the group containing halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group;
wherein heterocycle denotes a heterocyclic group containing 4 to 9 carbon atoms and at least one heteroatom selected from the group containing oxygen atom, sulphur atom, and nitrogen atom (e.g., thienyl, furyl, pyranyl, pyrrolyl, imidazolyl, pyrrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, isothiazolyl, isoxazyl, benzothienyl, naphthothienyl, benzofuranyl, chromenyl, indolyl, isoindolyl, indazolyl, quinolyl, isoquinolyl, phtalazinyl, quinoxalinyl, cinnolinyl, or quinazolinyl), which is optionally substituted independently with 1 to 7 substituents selected from the group containing alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heteroaryl denotes a heterocycle in which at least one heterocyclic ring is aromatic which is optionally

substituted independently with 1 to 7 substituents selected from the group containing alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heterocycloalkyl denotes a -R_a-Het group where Het is a heterocycle group and R_a is an alkyl group which can be optionally substituted independently with 1 to 7 substituents selected from the group containing alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heteroarylalkyl denotes a -R_a-HetAr group where HetAr is an heteroaryl group and R_a is as defined above;
wherein arylalkyl denotes a -R_b-Ar group where Ar is aryl group and R_b is a branched or unbranched alkyl chain containing 1 to 6 carbon atoms, the aryl group being substituted independently with 1 to 5 substituents selected from the group containing alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group;
wherein halogen denotes a fluorine, bromine, chlorine, or iodine atom,
wherein hydroxy denotes an -OH group,
wherein mercapto denotes a -SH group,
wherein amino denotes a -NH_2 group,
wherein carbamoyl denotes a -$CONH_2$ group.
wherein cyano denotes a -CN group,
wherein carboxyl denotes a -COOH group,
wherein nitro denotes a -NO_2 group,
wherein sulpho denotes a -SO_3R_c group where R_c is hydrogen or alkyl,
wherein sulphamido denotes the $SO_2NR_cR_c$' group where R_c and R_c' are independently hydrogen or alkyl,
wherein acyl denotes a -$C(O)R_d$ group, wherein R_d is alkyl, aryl, arylalkyl or cycloalkyl,
wherein acyloxy denotes a -O-$C(O)R_e$ group where R_e is alkyl, aryl, or heterocycle,
wherein acylamino denotes a -$NHCOR_f$ group, wherein R_f is alkyl, heterocycle, or aryl,
wherein alkyloxycarbonylamino denotes a -$NHCOOR_g$ group where R_g is alkyl or cycloalkyl,
wherein aryloxycarbonylamino denotes a -$NHCOOR_h$ group where R_h is aryl,
wherein alkyloxy denotes a -OR_h group where R_h is alkyl, cycloalkyl, or arylalkyl,
wherein aryloxy denotes a -OR_g group where R_g is aryl,
wherein alkylamino denotes a -NR_iR_j group where R_i is hydrogen, alkyl, or heterocycle and R_j is alkyl or heterocycle,
wherein arylamino denotes a -NR_kR_h group where R_k is hydrogen or aryl and R_h is alkyl, aryl, or heterocycle,
wherein alkylthio denotes a -SR_h group where R_h is as defined above, and
wherein arylthio denotes a -SR_g group where R_g is as defined above.

[0008] Preferred 6,9-disubstituted purine derivatives include 6-(2-hydroxycyclopropylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxycyclobutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxycyclohexylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-5-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,3-dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,4-dihydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,5-dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dihydroxy-4-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tet-

rahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-5-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dimethyl-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dibromo-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxymethyl-3-methylallyl)amino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(Z)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(1'-methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-4-morfolinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-1-pyrolidinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-6-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-carboxy-4-hydroxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methoxylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine and their pharmaceutically acceptable salts.

[0009] Particularly preferred 6,9-disubstituted purine derivatives include 6-(4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(1'-methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, and their pharmaceutically acceptable salts.

[0010] Another aspect of the invention are the 6,9-disubstituted purine derivatives of general formula I for use as cosmetics for inhibiting ageing and senescence of mammalian cells, especially epidermal cells such as keratinocytes or fibroblasts.

[0011] A further aspect of the invention are the 6,9-disubstituted purine derivatives of the general formula I for treating skin disease states (e.g., lupus, allergic eczema, toxic eczema, atopic dermatitis, ichtyosis, papilloma, Bowen's disease, seborrhoic keratosis, actinic keratosis, basal and squamous cell carcinoma, and the like).

[0012] Another aspect of the invention are the 6,9-disubstituted purine derivatives of the general formula I for treating inflammation, treating or accelerating the healing of lesions, and providing substantially immediate relief of pain and/or other immunological responses resulting from inflammation.

[0013] In a preferred embodiment, the 6,9-disubstituted purine derivatives of the general formula I are used for treating inflammation skin diseases as atopic dermatitis, lichen planus, hyperpigmentation, and Herpes simplex lesions.

[0014] The present invention provides a composition comprising one or more 6,9-disubstituted purine derivatives of the general formula I or their pharmaceutically acceptable salts thereof; especially preferred pharmaceutically acceptable salts are formed with alkali metals, ammonium or amines and may be in the forms of racemates, optically active isomers, or their addition salts with acids. Such compositions may contain other components so long as they are acceptable for application to mammalia cells and do not adversely effect or interfere with the activities of the one or more 6,9-disubstituted purine derivatives; these components can include, but are not limited to, one or more excipients and/or Ingredients normally used in cosmetic products.

[0015] A further aspect of the invention is the composition comprising one or more 6,9-disubstituted purine derivatives of the general formula I or the pharmaceutically acceptable salts thereof with alkali metals, ammonium or amines, in the forms of racemates or optically active isomers, or their addition salts with acids, and one or more excipients destined

for inhibiting ageing and senescence of mammalian epidermal cells, such as keratinocytes or fibroblasts.

[0016] A further aspect of the invention is the composition comprising one or more 6,9-disubstituted purine derivatives of the general formula I or the pharmaceutically acceptable salts thereof with alkali metals, ammonium or amines, in the forms of racemates or optically active isomers, or their addition salts with acids, and one or more excipients destined for treating skin disease states.

[0017] In a preferred embodiment, the object of the invention is the composition comprising one or more 6,9-disubstituted purine derivatives of the general formula I or the pharmaceutically acceptable salts thereof with alkali metals, ammonium or amines, In the forms of racemates or optically active isomers, or their addition salts with acids, and one or more excipients, destined for treating lupus, allergic eczema, toxic eczema, atopic dermatitis, ichtyosis, papilloma, Bowen's disease, seborrhoic keratosis, actinic keratosis, basal and squamous cell carcinoma.

[0018] Another aspect of the invention is the composition comprising one or more 6,9-disubstituted purine derivatives of the general formula I or the pharmaceutically acceptable salts thereof with alkali metals, ammonium or amines, in the forms of racemates or optically active isomers, or their addition salts with acids, and one or more excipients destined for treating the inflammation, to accelerate healing of lesions, and to provide substantially immediate relief of pain and other immunological responses resulting from inflammation.

[0019] The compositions of the present invention are useful for inhibiting ageing and/or senescence, improving the cosmetic appearance of mammalian cells (especially epidermal cells such as keratinocytes or fibroblasts) and/or mammalian skin, and/or ameliorating the adverse effect of aging in mammalian cells (especially epidermal cells such as keratinocytes or fibroblasts). For purposes of this invention, "inhibiting" is intended to include slowing, reversing, or stopping the development of undesirable cosmetic features, or otherwise improving the cosmetic appearance. These compositions are particularly useful for inhibiting ageing and senescence and/or improving the cosmetic appearance of human epidermal cells and/or human skin.

[0020] The compositions of the present invention are also useful for treatment of certain skin disease states, such as lupus, allergic eczema, toxic eczema, atopic dermatitis, ichtyosis, papilloma, Bowen's disease, seborrhoic keratosis, actinic keratosis, basal and squamous cell carcinoma, and the like.

[0021] The compositions of the present invention are also useful for treating Inflammation-related conditions, such as inflammation, lesions (e.g., accelerating healing thereof), pain and/or other immunological responses resulting from, or related to, inflammation (e.g., providing relief thereof) and/or treating inflammation skin diseases (e.g., atopic dermatitis, lichen planus, hyperpigmentation, Herpes simplex lesions, and the like).

[0022] The present invention further provides the 6,9 disubstituted purine derivatives of the general formula (I) for use in a method for ameliorating the adverse effect of aging in mammalian cells (especially epidermal cells such as keratinocytes or fibroblasts), said method comprising applying an effective amount of a novel 6,9-disubstituted purine derivative of this invention to the mammalian cells. Topically application to human skin is an especially preferred embodiment.

[0023] The present invention further provides the 6,9 disubstituted purine derivatives of the general formula (I) for use in a method for treating disease states in a mammal, said method comprising applying an effective amount of a novel 6,9-disubstituted purine derivative of this invention to the mammalian cells.

[0024] The present invention further provides the 6,9 disubstituted purine derivatives of the general formula (I) for use in a method for treating an inflammation condition in mammal, said method comprising applying an effective amount of a novel 6,9-disubstituted purine derivative of this invention to mammalian cells.

[0025] COMPOSITIONS. The cosmetic compositions of this Invention generally comprise from about 0.05 % (w/w) to about 10 % (w/w) of the active ingredient (i.e., one or more 6,9-disubstituted purine derivatives as described herein), preferably from about 0.1 % (w/w) to about 2 % (w/w). The cosmetic compositions can be in the form of a cream, an aerosol, a milky lotion, a lotion, a plaster, a poultice, a shampoo, a lipstick, an ointment, a paste, foam, a tincture, a spray, or the like.

[0026] Ointments are oil-in-water emulsions, which comprise not more than 70 %, but preferably 20 - 50 % of water or aqueous phase. The fatty phase consists of, in particular, hydrocarbons, for example vaseline, paraffin oil or hard paraffins, which preferably comprise suitable hydroxy compounds, such as fatty alcohols or esters thereof, for example cetyl alcohol or wool wax alcohols, such as wool wax, to improve the water-binding capacity. Emulsifiers are lipophilic substances, such as sorbitan fatty acid esters (Spans), for example sorbitan oleate and/or sorbitan isostearate. Additives to the aqueous phase are, for example, humectants, such as polyalcohols, for example glycerol, propylene glycol, sorbitol and/or polyethylene glycol, or preservatives and odoriferous substances.

[0027] Fatty ointments are anhydrous and comprise, as the base, in particular, hydrocarbons, for example paraffin, vaseline or paraffin oil, and furthermore naturally occurring or semi-synthetic fats, for example hydrogenated coconut-fatty acid triglycerides, or, preferably, hydrogenated oils, for example hydrogenated groundnut or castor oil, and furthermore fatty acid partial esters of glycerol, for example glycerol mono- and/or distearate, and for example, fatty alcohols. They also contain emulsifiers and/or additives mentioned in connection with the ointments which increase the uptake of water.

[0028] Creams are oil-in-water emulsions, which comprise more than 50 % of water. Oily bases used are, in particular,

fatty alcohols, for example lauryl, cetyl or stearyl alcohols, fatty acids, for example palmitic or stearic acid, liquid to solid waxes, for example isopropyl myristate, wool wax or beeswax, and/or hydrocarbons, for example vaseline (petrolatum) or paraffin oil. Emulsifiers are surface-active substances with predominantly hydrophilic properties, such as non-ionic emulsifiers, for example fatty acid esters of polyalcohols or ethyleneoxy adducts thereof, such as polyglyceric fatty acid esters or polyethylene sorbitan fatty esters (Tweens), and furthermore polyoxyethylene fatty alcohol ethers or polyoxyethylene fatty acid esters, or ionic emulsifiers, such as alkali metal salts of fatty alcohol sulphates, for example sodium lauryl sulphate, sodium cetyl sulphate or sodium stearyl sulphate, which are usually used in the presence of fatty alcohols, for example cetyl stearyl alcohol or stearyl alcohol. Additives to the aqueous phase are, inter alia, agents which prevent the creams from drying out, for example polyalcohols, such as glycerol, sorbitol, propylene glycol and/or polyethylene glycols, and furthermore preservatives and odoriferous substances.

[0029] Pastes are creams and ointments containing secretion-absorbing powder constituents, such as metal oxides, for example titanium oxide or zinc oxide, and in addition talc and/or aluminium silicates, which have the task of binding the moisture or secretions present.

[0030] Suspensions in oil comprise, as the oily component, the vegetable, synthetic or semisynthetic oils. Oils which may be mentioned are, in particular, liquid fatty acid esters which contain, as the acid component, a long-chain fatty acid having 8-22, in particular 12-22, carbon atoms, for example lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, arachidonic acid, behenic acid or unsaturated acids, for example oleic acid, elaidic acid, euric acid, brasidic acid or linoleic acid, if appropriate with the addition of antioxidants, for example vitamin E, b-carotene or 3,5-di-tert-butyl-4-hydroxytoluene. The alcohol component of these fatty acid esters has not more than 6 carbon atoms and is mono- or polyhydric, for example mono-, di- or trihydric alcohol, for example methanol, ethanol, propanol, butanol, or pentanol, or isomers thereof, but in particular glycol and glycerol. Fatty acid esters are therefore, for example: ethyl oleate, isopropyl myristate, isopropyl palmitate, "Labrafil M 2375" (polyoxyethylene glycerol trioleate from Gattefosé, Paris), "Labrafil M 1944 CS" (unsaturated polyglycolated glycerides prepared by an alcoholysis of apricot kernel oil and made up of glycerides and polyethylene glycol esters; from Gattefosé, Paris), "Labrasol" (saturated polyglycolated glycerides prepared by an alcoholysis of TCM and made up of glycerides and polyethylene glycol esters; from Gattefosé, Paris) and/or "Miglyol 812" (triglyceride of saturated fatty acids of chain length C_8 to C_{12} from Hüls AG, Germany), and in particular vegetable oils, such as cottonseed oil, almond oil, olive oil, castor oil, sesame oil, soybean oil and, In particular, groundnut oil.

[0031] Foams are administered from pressurised containers and they are liquid oil-in-water emulsions present in aerosol foam. As the propellant gases halogenated hydrocarbons, such as polyhalogenated alkanes, for example dichlorofluoromethane and dichlorotetrafluoroethane, or, preferably, non-halogenated gaseous hydrocarbons, air, N_2O, or carbon dioxide are used. The oily phases used are, inter alia, those mentioned above for ointments and creams, and the additives mentioned there are likewise used.

[0032] Tinctures and solutions usually comprise an aqueous-ethanolic base to which, humectants for reducing evaporation, such as polyalcohols, for example glycerol, glycols and/or polyethylene glycol, and re-oiling substances, such as fatty acid esters with lower polyethylene glycols, i.e., lipophilic substances soluble in the aqueous mixture to substitute the fatty substances removed from the skin with the ethanol, and, if necessary, other excipients and additives are admixed.

[0033] The invention also relates to the 6,9 disubstituted purine derivatives of the general formula (I) for use in a process or method for the treatment of the cell senescence and the disease states mentioned above. The compounds can be administered prophylactically or therapeutically in the form of cosmetic compositions, preferably in an amount which is effective against the cell senescence or the disease states mentioned.

Examples

[0034] The invention is further illustrated by the following examples, which should not be construed as further limiting. Compounds not falling within general formula I are included in the Examples for comparison purposes.

[0035] The starting material for the compounds of the formula I is 6-chloro-9-(tetrahydropyran-2-yl)purine, synthesised from 6-chloropurine and 3,4-dihydropyran using *p*-toluenesulfonic acid according to the literature (Robins et al., J. Am. Chem. Soc. 83, 2574 (1961)). Starting substituted benzylamines, not commercially available (otherwise obtained *via* Sigma Aldrich or Fluorochem), were prepared from the corresponding aldehydes In the presence of a suitable metal catalyst. 3-Methyl-but-2-enylamine was prepared by a three-step synthesis from the corresponding halide using the Gabriel synthesis. 4-Hydroxy-3-methyl-E-but-2-enyl-amine was prepared by a five-step synthesis from isoprene according to the literature (Ohsugi et al., Agr. Biol. Chem., 38 (10), 1925, (1974)).

[0036] Elemental analyses (C, H and N) were performed on the EA1108 CHN analyser (Fissons Instruments). The melting points were determined on the BÜCHI Melting Point B-540 apparatus and are uncorrected. Analytical thin layer chromatography (TLC) was carried out using silica gel 60 WF_{254} plates (Merck), solvent $CHCl_3$:MEOH:conc. NH_4OH (8:2:0.2, v/v/v). ES+ mass spectra were recorded using direct probe on the Waters ZMD 2000 mass spectrometer. The mass monitoring interval was 10 - 1500 amu. The spectra were collected using 3.0 second cyclic scans and applying a

sample cone voltage of 25 V at source block temperature 150 °C, desolvation temperature 80 °C and desolvation gas flow rate 200 l/hour. The mass spectrometer was directly coupled to a MassLynx data system. NMR spectra were measured on the Bruker Avance AV 300 spectrometer operating at a temperature of 300 K and a frequency of 300.13 MHz (^{1}H) and 75.48 MHz (^{13}C), respectively. Samples were prepared by dissolving the compounds in DMSO-d_6. Tetramethylsilane (TMS) was used as the internal standard.

[0037] EXAMPLE 1: 6-(4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl)purine. A mixture of 10 mmol (2387 mg) 6-chloro-9-(tetrahydropyran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1478 mg) 4-hydroxybenzylamine, and 5 mL of triethylamine was refluxed in *n*-propanol for 3 hours. After removal of the *n*-propanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate solvent was evaporated and the residuum subsequently washed with 30 ml of diethylether. The solid residue was filtered off and the crude product crystallized from methanol. Yield 80 %, white solid. TLC (EtOAc:hexane (1:1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H-NMR (400 MHZ, DMSO): 1.57tt(2H, J_a = 11.0 Hz, J_b = 3.3 Hz); 1.72qq(1H, J_a = 12 Hz, J_b = 3.3 Hz); 1.95tt(2H, J_a = 11 Hz, J_b = 2.1 Hz); 2.27qq (1H, J_a = 12.0 Hz, J_b = 3.3 Hz); 3.67m(1 H); 4.0dd(1H, J_a = 11.0 Hz, J_b = 2.1 Hz); 4.6s(2H); 5.63dd(1H, J_a = 11.0 Hz, J_b = 2.1 Hz); 6.67d(2H, J = 8.4Hz); 7.15d(2H, J = 8.4 Hz); 8.02bs (1H); 8.21s(1H); 8.33s(1 H); 9.21s(1H). MS (ES): $[M+H]^+$= 326 (100).

[0038] EXAMPLE 2: 6-(3-hydroxybenzylamino)-9-(tetrahydropyran-2-yl)purine. A mixture of 10 mmol (2387 mg) 6-chloro-9-(tetrahydropyran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1478 mg) 3-hydroxybenzylamine, and 5 mL of triethylamine was refluxed in *n*-butanol for 3 hours. After removal of the *n*-butanol by vacuum evaporation water was added to remove the *n*-butanol residues. The resulting material was treated with water and partitioned into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of diethylether. The solid residue was filtered off and the crude product crystallized from methanol. Yield 90 %, white solid. TLC (EtOAc:hexane (1:1) (v:v): single spot; HPLC: purity> 99 %. ^{1}H-NMR (400 MHZ, DMSO): 1.57m(2H); 1.70m(1H); 1.95m(2H); 2.27qq (1H, J_a = 11.7 Hz, J_b = 4.0 Hz); 3.66m(1H); 4.0d(1H); 4.63bs(2H); 5.67dd(1H, J_a = 11.3 Hz, J_b = 1.8 Hz); 6.58dd(1H, J_a = 8.2 Hz, J_b = 1.5 Hz); 6.73(d, 1H, J = 7.7 Hz); 7.07t(1 H, J = 7.7 Hz); 8.21s (1H); 8.33bs (1 H); 8.36bs(1 H); 9.26s(1 H). MS (ES): $[M+H]^+$= 326 (100).

[0039] EXAMPLE 3: 6-(2-hydroxybenzylamino)-9-(tetrahydropyran-2-yl)purine. A mixture of 10 mmol (2387 mg) 6-chloro-9-(tetrahydropyran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1478 mg) 2-hydroxybenzylamine, and 5 mL of triethylamine was refluxed in *n*-propanol for 3 hrs. After removal of the *n*-propanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate solvent was evaporated and the residuum subsequently washed with 30 ml of diethylether. The solid residue was filtered off and the crude product crystallized from methanol. Yield 90 %, white solid. TLC (EtOAc:hexane (1:1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H-NMR (400 MHZ, DMSO): 1.58m(2H); 1.70m(1 H); 1.95m(2H); 2.26qq (1 H, J_a = 11.8 Hz, J_b = 4.0 Hz); 3.67m(1 H); 4.0d(1 H, J = 11.3 Hz); 4.64bs(2H); 5.63dd(1H, J_a = 11.3 Hz, J_b = 1.8 Hz); 6.73t(1H, J = 7.5 Hz); 6.82(d, 1H, J = 7.9 Hz); 7.06t(1H, J = 7.5 Hz); 7.14d(1H, J = 7.5 Hz); 8.21s (1H); 8.35bs(1H); 8.37bs(1H); 9.82bs(1H). MS (ES): $[M+H]^+$= 326 (100).

[0040] EXAMPLE 4: 6-(2,3-dihydroxybenzylamino)-9-(tetrahydropyran-2-yl)purine. A mixture of 10 mmol (2387 mg) 6-chloro-9-(tetrahydropyran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (2100 mg) 2,3dihydroxybenzylamine hydrochloride, and 7 mL of triethylamine was refluxed in *n*-propanol for 3 hrs. After removal of the *n*-propanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate solvent was evaporated and the residuum subsequently washed with 30 ml of petroleum ether. The solid residue was filtered off and the crude product crystallized from methanol. Yield 60 %, white solid. TLC ($CHCl_3$: methanol) (4:1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H-NMR (300 MHz, DMSO): 1.57m(2H); 1.71m(1H); 1.95m(2H); 2.27qq(1 H, J_a = 12 Hz, J_b = 4.0 Hz); 3.67m(1H); 4.00d(1H, J = *11.7* Hz); 4.58bs(2H); 5.63dd(1H, J_a = 11.2 Hz, J_b = 1.9 Hz); 6.55tt(1H, J_a = 7.7 Hz, J_b = 1.5 Hz); 6.63dd(1H, J_a = 7.7 Hz, J_b = 1.8 Hz); 6.66dd(1H, J_a = 7.7 Hz, J_b = 1.8 Hz); 8.24s(1H); 8.27bs(1H); 8.37s(1 H), 8.96bs(1H), 9.53bs(1H). MS (ES): $[M+H]^+$= 342 (100).

[0041] EXAMPLE 5: 6-(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl)purine. A mixture of 10 mmol (2387 mg) 6-chloro-9-(tetrahydropyran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1754 mg) (E)-(4-hydroxy-3-methylbut-2-en-1-ylamine hemioxalate and 3 mL of triethylamine was refluxed in *n*-butanol for 3 hrs. After removal of the *n*-butanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of diethylether. The solid residue was filtered off and the crude product crystallized from methanol. Yeld 75 %, white solid. TLC ($CHCl_3$:methanol (4:1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H-NMR (400 MHz, DMSO): 1.36m(2H); 1.66s (3H); 1.71m(1H); 1.94m(2H); 2.25m(1H); 3.67m(1H); 3.78d(2H, J =5.7 Hz); 4.00d(1H, J = 10.8 Hz); 4.14bs(2H); 4.71t (1 H, J = 5.7 Hz); 5.52t(1 H, J =6.0 Hz); 5.61dd(1H, J_a = 10.8 Hz, J_b = 2.0 Hz); 7.83bs(1H); 8.21s(1H); 8.31bs(1H). MS (ES): $[M+H]^+$= 304 (100).

[0042] EXAMPLE 6: 6-(4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl)purine. A mixture of 10 mmol (2387 mg) 6-chloro-9-(tetrahydropyran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (2318 mg) 4-hydroxy-3-methylbutylamine oxalate, and 5 mL of triethylamine was refluxed in *n*-propanol for 3 hours and subsequently

24 hrs at laboratory temperature. After removal of the *n*-propanol by vacuum evaporation, the resulting material was treated with water and partitioned into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of hexane. The solid residue was filtered off and the crude product crystallized from methanol. Yield 75 %, white solid. TLC ($CHCl_3$:methanol (4:1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H-NMR (400 MHz, DMSO): 0.88d(3H, *J* = 6.6 Hz); 1.34m(1H); 1.56m(3H); 1.70m(1H); 1.71m(1H); 1.93m(2H); 1.94m(1H); 2.26m(1H); 3.25m(1H); 3.52bs(2H); 3.67m(1H); 4.0d(1H, *J* = 11.3 Hz); 4.42t(1 H, *J* =5.1 Hz); 5.61d(1H, *J* = 10.6 Hz); 7.10bs(1H); 8.20s(1H); 8.30s(1 H). MS (ES): $[M+H]^+$= 306 (100).

[0043] EXAMPLE 7: 6-(4-hydroxyanilino)-9-(tetrahydropyran-2-yl)-purine. A mixture of 10 mmol (2387 mg) 6-chloro-9-(tetrahydropyran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1309 mg) of 4-hydroxyphenylamine (4-hydroxyaniline) and 4 ml of N-ethyldiisopropylamine was refluxed in *n*-butanol for 3 hrs. After removal of the *n*-butanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate solvent was evaporated and the residuum subsequently washed with 30 ml of ether. The solid residue was filtered off and the crude product crystallized from methanol. Yield: 90 %, white solid. TLC ($CHCl_3$:CH_3OH:NH_3) (90:10:0.1) (v:v): single spot; HPLC: purity > 98 %. ^{1}H NMR (400 MHz, DMSO): 1.56tt(2H, J_a = 11.0 Hz, J_b = 3.3 Hz); 1.72qq(1H, J_a = 11.6 Hz, J_b = 3.3 Hz); 1.94tt(2H, J_a = 11.0 Hz, J_b = 3.3 Hz); 2.28qq(1 H, J_a = 11.6 Hz, J_b = 3.3 Hz); 3.66m(1 H); 3.98dd(1H, J_a = 11.0 Hz, J_b = 2.1 Hz); 5.62dd(1H, J_a = 11.0 Hz, J_b = 2.1 Hz); 7.02d(2H, J =8.5 Hz); 8.19s (1H); 8.26d(2H, J = 8.5 Hz); 8.29s(1H); 8.95s(1H). MS (ES^+): $[M+H]^+$= 312 (100).

Table 1: Compounds prepared by the method of examples 1-7

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES - ZMD	
	R6	R9		$[M-H]^{-}$ a)	$[M+H]^{+}$ b)
1	(E)-(4-hydroxy-2-methylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	C=59,0; H=6,7; N=23.6	302	304
2	(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	C=59,8; H=6,9; N=23,5	302	304
3	(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	C=59,6; H=6,9; N=22,8	302	304
4	(Z)-(4-hydroxy-1,3-dimethylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	C=60,0; H=7,4; N=22,4	316	318
5	(E)-(4-hydroxy-1,3-dimethylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	C=60,4; H=7,5; N=22,4	316	318
6	4-hydroxy-3-methylbutylamino	tetrahydropyran-2-yl	C=58,9; H=7,5; N=23,0	304	306
7	4-hydroxybut-2-en-1-ylamino	tetrahydropyran-2-yl	C=58,1; H=6,6; N=24,2	288	290
8	2-hydroxybenzylamino	tetrahydropyran-2-yl	C=62,4; H=5,9; N=21,3	324	326
9	3-hydroxybenzylamino	tetrahydropyran-2-yl	C=62,8; H=5,9; N=21,3	324	326
10	4- hydroxybenzylamino	tetrahydropyran-2-yl	C=62,7; H=5,8; N=21,6	324	326
11	2-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	C=63,6; H=6,3; N=20,2	354	356
12	2-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	C=63,6; H=6,3; N=20,3	354	356
13	2-hydroxy-5-methoxybenzylamino	tetrahydropyran-2-yl	C=63,6; H=6,3; N=20,2	354	356
14	2,3-dihydroxybenzylamino	tetrahydropyran-2-yl	C=59,9; H=5,7; N=20,7	340	342
15	2,4-dihydroxybenzylamino	tetrahydropyran-2-yl	C=59,7; H=5,6; N=20,5	340	342
16	2,5-dihydroxybenzylamino	tetrahydropyran-2-yl	C=60,0; H=5,7; N=20,6	340	342

(continued)

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES - ZMD	
	R6	R9		[M-H]$^{-}$ a)	[M+H]$^{+}$ b)
17	2,6-dihydroxybenzylamino	tetrahydropyran-2-yl	C=59,5; H=5,6; N=20,9	340	342
18	3,4-dihydroxybenzylamino	tetrahydropyran-2-yl	C=60,1; H=5,7 N=20,6	340	342
19	3,5-dihydroxybenzylamino	tetrahydropyran-2-yl	C=60,1; H=5,6; N=20,7	340	342
20	4-hydroxy-3,5-dimethoxybenzylamino	tetrahydropyran-2-yl	C=59,1; H=5,8; N=18,4	384	386
21	4 hydroxy 2 6-dimethoxybenzylamino	tetrahydropyran-2-yl	C=59,1; H=5,9; N=18,6	384	386
22	4-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	C-63,6; H=6,3; N-20 2	354	356
23	3-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	C-63,5; H=6,3; N=20,2	354	356
24	2,3,4-trihydroxybenzylamino	tetrahydropyran-2-yl	C=57,2; H=5,4; N=19,7	356	358
25	2,4,5-trihydroxybenzylamino	tetrahydropyran-2-yl	C=57,2; H-5 2 N=20,2	356	358
26	2-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	C=63,4; H=6,3; N=20,2	338	340
27	2-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	C=63,1; H=6,4; H=6,4; N=20,4	338	340
28	4-hydroxy-3-mathylbenzylamino	tetrahydropyran-2-yl	C=63,5; H=6 3 N=20 5	338	340
29	4-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	C=63,7; H=6,4; N=20,4	338	340
30	3-hydroxyfurfurylamino	tetrahydropyran-2-yl	C=57,0; H=5 3; N=22,4	314	310
31	4-hydroxyfurfurylamino	tetrahydropyran-2-yl	C=57,0; H=5,4; N=22,3	314	316
32	5-hydroxyfurfurylamino	tetrahydropyran-2-yl	C=57,1; H=5,4; N=22,3	314	316
33	5-hydroxy-pent-2-en-1-yl	tetrahydropyran-2-yl	C=59,4; H=6,9; N-23,1	302	304
34	2-hydroxyanilino	tetrahydropyran-2-yl	C=61,6; H-5,6; N=22,8	310	312
35	3-hydroxyinilino	tetrahydropyran-2-yl	C=61,6; H-5,5; N=23,0	310	312
36	4-hydroxyanilino	tetrahydropyran-2-yl	C=61,2; H=5,5; N=22,6	310	312
37	4-hydroxy-3-methylanilino	tetrahydropyran-2-yl	C=62,7; H=5,9; N=21,7	324	326
38	4-hydroxy-5-methylanilino	tetrahydropyran-2-yl	C=62,8; H=5,9; N=21,7	324	326
39	2 4-dihydroxyanilino	tetrahydropyran-2-yl	C=58,6; H=5,2; N=21,7	326	328
40	3,4-dihydroxyanilino	tetrahydropyran-2-yl	C=58,5; H=5,2; N=21,1	326	328
41	4-hydroxy-3,5-dimethoxyanilino	tetrahydropyran-2-yl	C=58,0; H=5,8; N=19,1	370	372
42	4-hydroxy-2,6-dimethoxyanilino	tetrahydropyran-2-yl	C=57,7; H=5,8; N=19,1	370	372
43	3-hydroxy-4-methoxyanilino	tetrahydropyran-2-yl	C=59,6; H=5,6; N=20,8	340	342
44	2,3,4-trihydroxyanilino	tetrahydropyran-2-yl	C=5,7; H=5,1; N=20,9	342	344

(continued)

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES - ZMD	
	R6	R9		$[M-H]^{-}$ a)	$[M+H]^{+}$ b)
45	4-hydroxy-3-methoxyanilino	tetrahydropyran-2-yl	C=59,8; H=5,6; N=20,5	340	342
46	1-methyl-4-hydroxy-3-methylbutylamino	tetrahydropyran-2-yl	C=60.2; H=7,9; N=21,9	318	320
a) solution: MeOH p a + HCOOH b) solution: MeOH p.a. + H_2O + NH_3					

[0044] EXAMPLE 8: 6-(4-hydroxybenzylamino)-9-(tetrahydrofuran-2-yl)-purine. A mixture of 10 mmol (2240 mg) of 6-chloro-9-(tetrahydrofuran-2-yl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1478 mg) of 4-hydroxybenzylamine, and 5 ml of N-ethyldiisopropylamine was refluxed in *n*-propanol for 3 hours. After removal of the *n*-propanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of petroleum ether. The solid residue was filtered off and the crude product crystallized from methanol. Yield 80 %, white solid. TLC (EtOAc:hexane (1:1 (v:v)): single spot; HPLC: purity> 98 %. ^{1}H NMR (400 MHZ, DMSO): 1.36tt(2H, J_a= 7.8 Hz, J_b= 2.2 Hz); 2.23m(1H); 2.32m(1 H); 3.62dd(1H, J_a= 10.8 Hz, J_b= 3.8 Hz); 3.87dd (1H, J_a=10.8 Hz, J_b=*3.8* Hz); 4.62s(2H); 6.23dd(1H, J_a=5.3 Hz, J_b=1.5 Hz); 6.71d(2H, *J*= 8.3 Hz); 7.21 d(2H, J = 8.3 Hz); 8.06bs(1H); 8.16s(1H); 8.28s(1 H); 9.23s(1 H). MS (ES): $[M+H]^+$= 312 (100). EXAMPLE 9: 6-(3-hydroxybenzylamino)-9-(tetrahydrofuran-2-yl)-purine. A mixture of 10 mmol (2240 mg) of 6-chloro-9-(tetrahydrofuran-2-yl)-purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1478 mg) of 3-hydroxybenzylamine, and 5 ml of N-ethyldiisopropylamine was refluxed in n-propanol for 3 hours. After removal of the *n*-propanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of petroleum ether. The solid residue was filtered off and the crude product crystallized from methanol. Yield 85 %, white solid. TLC (EtOAc: hexane (1:1 (v:v)): single spot; HPLC: purity> 98 %. ^{1}H NMR (400 MHZ, DMSO): 2.20sep(1H, *J* = 6.8 Hz); 2.22sep(1H, *J*= 6.8 Hz); 2.44m(2H); 3.91q(1H, *J*= 7.3 Hz); 4.14q(1H, *J* = 7.3 Hz); 4.63bs(2H); 6.26m(1 H); 6.59dd(1 H, J_a = 7.8 Hz, J_b = 2.2 Hz); 6.73s(1H); 6.75d(1H, *J* = 7.8 Hz); 7.07t(1 H, *J* = 7.8 Hz); 8.20s(1H); 8.26bs(1 H); 8.27s(1H); 9.23bs(1 H). MS (ES): $[M+H]^+$= 312 (100).

[0045] EXAMPLE 10: 6-(2-hydroxybenzylamino)-9-(tetrahydrofuran-2-yl)-purine. A mixture of 10 mmol (2240 mg) of 6-chloro-9-(tetrahydrofuran-2-yl)-purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1478 mg) of 2-hydroxybenzylamine, and 5 ml of triethylamine was refluxed in *n*-propanol for 3 hours. After removal of the *n*-propanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of petroleum ether. The solid residue was filtered off and the crude product crystallize from methanol. Yield 80 %, white solid. TLC (EtOAc:hexane) (1:1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H NMR (400 MHZ, DMSO): 2.22sep(1H); 2.44m(1 H); 3.82q(1 H, *J* = 7.3 Hz); 4.15q (1H, *J* = 7.3 Hz); 4.69bs(2H); 6.26m(1H); 6.73t(1H, *J* = 7.5 Hz); 6.82d(1H, *J* = 7.9 Hz); 7.06t(1 H, *J* = 7.8 Hz); 7.17d(1H, *J* = 7.3 Hz); 8.05bs(1H); 8.22s(1H); 8.23s(1H); 9.82bs(1H). MS (ES): $[M+H]^+$= 312 (100).

[0046] EXAMPLE 11: 6-(4-hydroxy-3-methoxybenzylamino)-9-(tetrahydrofuran-2-yl)-purine. A mixture of 10 mmol (2240 mg) of 6-chloro-9-(tetrahydrofuran-2-yl)-purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1838 mg) of 4-hydroxy-3-methoxybenzylamine and 5 mL of triethylamine was refluxed in *n*-propanol for 3 hours. After removal of the n-propanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of petroleum ether. The solid residue was filtered off and the crude product crystallized from methanol. Yield 80 %, white solid. TLC (EtOAc: hexane) (1:1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H NMR (400 MHZ, DMSO): 0.90d(3H, J = 6.6 Hz); 1.32m(1H); 1.57m(1H); 1.84m(1H); 1.95m(1H); 2.12m(2H); 2.29m(1 H); 3.26m(1H); 3.51 bs(2H); 3.73m(1 H); 3.89m(1 H); 4.40t(1 H, J = 5.1 Hz); 6.12d(1H, J = 5.2 Hz); 7.74bs(1H); 8.18s(1H); 8.28s(1H: MS (ES): $[M+H]^+$= 342 (100).

Table 2: Compounds prepared by the method of example 8-11;

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES-ZMD	
	R6	R9		$[M-H]^{-}$ a)	$[M-H]^{+}$ b)
47	(E)-(4-hydroxy-2-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	C=57,7; H=6,3; N=24,7	288	290

(continued)

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES-ZMD	
	R6	R9		[M-H]$^{-}$ a)	[M-H]$^{+}$ b)
47	(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	C=58,6; H=6,8; N=23,9	288	290
49	(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	C=57,9; H=6,4; N=24,5	288	290
50	(Z)-(4-hydroxy-1,3-dimethylbut-2-en-1-ylamino)	tetrahydrofuren-2-yl	C=59,0; H=7,2; N=23,1	302	304
51	(E)-(4-hydroxy-1,3-dimethylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	C=59,0; H=7,2; N=23,3	302	304
52	4-hydroxy-3-methylbutylamino	tetrahydrofuran-2-yl	C=57,8; H=7,3; N=24,1	290	292
53	1-methyl-4-hydroxy-3-methylbutylamino	tetrahydrofuran-2-yl	C=59.0; H=7,6; N=22,9	304	306
54	4-hydroxybut-2-en-1-ylamino	tetrahydrofuran-2-yl	C=56,7; H=6,2; N=25,4	274	276
55	2-hydroxybenzylamino	tetrahydrofuran-2-yl	C=61,5; H=5,5; N=22,7	310	312
56	3-hydroxybenzylamino	tetrahydrofuran-2-yl	C=61,5; H=5,4; N=22,5	310	312
57	4- hydroxybenzylamino	tetrahydrofuran-2-yl	C=61,5; H=5,4; N=22,7	310	312
58	2-hydroxy-3-methoxybenzylamino	tetrahydrofuran-2-yl	C=59,7; H=5,1; N=21,0	340	342
59	2-hydroxy-4-methoxybenzylamino	tetrahydrofuran-2-yl	C=59,5; H=5,5; N=20,9	340	342
60	2-hydroxy-5-methoxybenzylamino	tetrahydrofuran-2-yl	C=59,6; H=5,5; N=20,7	340	342
61	2,3-dihydroxybenzylamino	tetrahydrofuran-2-yl	C=58,5; H=5,2; N=21,5	326	328
62	2,4-dihydroxybenzylamino	tetrahydrofuran-2-yl	C=58,7; H=5,1; N=21,5	326	328
63	2,5-dihydroxybenzylamino	tetrahydrofuran-2-yl	C=55,8; H=5,1; N=21,4	326	328
64	2,6-dihydroxybenzylamino	tetrahydrofuran-2-yl	C=58,5; H=5,1; N=21,7	326	328
65	3,4-dihydroxybenzylamino	tetrahydrofuran-2-yl	C=58,7; H=5,2; N=21,5	326	328
66	3,5-dihydroxybenzylamino	tetrahydrofuran-2-yl	C=58,5; H=5,1; N=21,5	326	328
67	4-hydroxy-3,5-dimethoxybenzylamino	tetrahydrofuran-2-yl	C=58,0; H=5,6; N=19,3	370	372
68	4-hydroxy-2.6-dimethoxybenzylamino	tetrahydrofuran-2-yl	C=57,7; H=5,6; N=19,5	370	372
69	4-hydroxy-3-methoxybenzylamino	tetrahydrofuran-2-yl	C=59,7; H=5,5; N=20,8	340	342
70	3-hydroxy-4-methoxybenzylamino	tetrahydrofuran-2-yl	C=59,8; H=5,6; N=20,6	340	342
71	2,3,4-trihydroxybenzylamino	tetrahydrofuran-2-yl	C=59,7; H=6,0; N=18,3	384	386
72	2,4,5-trihydroxybenzylamino	tetrahydrofuran-2-yl	C=59,2; H=6,1; N=18,7	384	386
73	2-hydroxy-3-methylbenzylamino	tetrahydrofuran-2-yl	C=62,5; H=6,0; N=22,0	324	326
74	2-hydroxy-5-methylbenzylamino	tetrahydrofuran-2-yl	C=62,1; H=5,8; N=21.9	324	326

(continued)

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES-ZMD	
	R6	R9		[M-H]$^{-}$ a)	[M-H]$^{+}$ b)
75	4-hydroxy-3-methylbenzylamino	tetrahydrofuran-2-yl	C=62,9; H=5,8; N=21,4	324	326
76	4-hydroxy-5-methylbenzylamino	tetrahydrofuran-2-yl	C=62,6; H=5,8; N=21,6	324	326
77	3-hydroxyfurfurylamino	tetrahydrofuran-2-yl	C=55,5; H=5,1; N=23,8	300	302
78	4-hydroxyfurfurylamino	tetrahydrofuran-2-yl	C=55,9; H=5,2; N=22,7	300	302
79	5-hydroxyfurfurylamino	tetrahydrofuran-2-yl	C=55,4; H=4,9; N=23,5	300	302
80	5-hydroxy-pent-2-en-1-yl	tetrahydrofuran-2-yl	C=58,1; H=6,6; N=24,2	288	290
81	2-hydroxyanilino	tetrahydrofuran-2-yl	C=60,3: H=5,0; N=23,6	296	298
82	3-hydroxyanilino	tetrahydrofuran-2-yl	C=60,1; H=5,1; N=23,7	296	298
83	4-hydroxyanilino	tetrahydrofuran-2-yl	C=60,4; H=5,0; N=23,7	296	298
84	4-hydroxy-3-methylanilino	tetrahydrofuran-2-yl	C=61,5; H=5,2; N=22,7	310	312
85	4-hydroxy-5-methylanilino	tetrahydrofuran-2-yl	C=61,6; H=5,2; N=22,8	310	312
86	2,4-dihydroxyanilino	tetrahydrofuran-2-yl	C=57,1; H=4,7; N=22,7	312	314
87	3,4-dihydroxyanilino	tetrahydrofuran-2-yl	C=57,4; H=4,8; N=22,3	312	314
88	4-hydroxy-3,5-dimethoxyanilino	tetrahydrofuran-2-yl	C=56,9; H=5,4; N=20,1	356	358
89	4-hydroxy-2,6-dimethoxyanilino	tetrahydrofuran-2-yl	C=57,0; H=5,6; N=19,9	356	358
90	3-hydroxy-4-methoxyanilino	tetrahydrofuran-2-yl	C=58,4; H=5,6; N=21,5	326	328
91	4-hydroxy-3-methoxyanilino	tetrahydrofuran-2-yl	C=58,7; H=5,2; N=21,4	326	328
92	2,3,4-trihydroxyanilino	tetrahydrofuran-2-yl	C=54,1; H=4,4; N=19,9	328	330
93	2,4,5-trihydroxyanilino	tetrahydrofuran-2-yl	C=54,3; H=4,3; N=19,8	328	330

a) solution: MeOH p.a. + HCOOH
b) solution: MeOH p.a. + H_2O + NH_3

[0047] EXAMPLE 12: 6-(4-hydroxybenzylamine)-9-(4-chlorobutyl)purine. A mixture of 10 mmol (2451 mg) of 6-chloro-9-(4-chlorobutyl)purine (prepared from 10 mmol (1546 mg) of 6-chloropurine), 12 mmol (1478 mg) of 4-hydroxybenzylamine and 5 mL of triethylamine was refluxed in *n*-butanol for 3 hrs. After removal of the *n*-butanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate solvent was evaporated and the residuum subsequently washed with 30 ml of diethylether. The solid residue was filtered off and crude product crystallized from methanol. Yield: 70 %, white solid. TLC ($CHCl_3$:CH_3OH:NH_3) (85:15:0.1) (v:v): single spot; HPLC: purity> 98 %. ^{1}H NMR (400 MHZ, DMSO): 1.89m(4H); 3.46dd(2H, J_a = 11.0 Hz, J_b = 3.6 Hz); 4.22tt(2H, J_a =13.0 Hz, J_b = 3.5 Hz); 4.61 s(2H); 6.59d (2H, J = 8.3 Hz); 7.27d(2H, J = 8.3 Hz); 8.18s(1H); 8.22bs(1H); 8.31 s(1H); 9.18s(1H). MS (ES): $[M+H]^+$= 346 (100).

Table 3: Compounds prepared by the method of example 12

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES - ZMD	
	R6	R9		[M-H]$^{-*}$ a)	[M+H]$^{+*}$ b)
94	(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	4-chlorobutyl	C=54,2; H=6,5; N=22,7	308	310

(continued)

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES - ZMD	
	R6	R9		$[M-H]^{-*}$ a)	$[M+H]^{+*}$ b)
95	(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	4-chlorobutyl	C=54,0; H=6,4; N=23,1	308	310
96	4-hydroxy-3-methylbutylamino	4-chlorobutyl	C=53,5; H=7,1; N=23,1	310	312
97	1-methyl-4-hydroxy-3-methylbutylamino	4-chlorobutyl	C=55,3; H=7,4; N=21,5	324	326
98	4-hydroxybut-2-en-1-ylamino	4-chlorobutyl	C=52,8; H=6,1; N=11,9	294	296
99	2-hydroxybenzylamino	4-chlorobutyl	C=57,5; H=5,5; N=21,2	344	346
100	3-hydroxybenzylamino	4-chlorobutyl	C=58,1; H=5,5; N=21,3	344	346
101	4- hydroxybenzylamino	4-chlorobutyl	C=57,8; H=5,4; N=21,7	344	346
102	2-hydroxy-3-methoxybenzylamino	4-chlorobutyl	C=55,9; H=5,5; N=19,9	360	362
103	2-hydroxy-4. methoxybenzylamino	4-chlorobutyl	C=56,1; H=5,6; N=19,7	360	362
104	2-hydroxyl-5-methoxybenzylamino	4-chlorobutyl	C=56,5; H=5,7; N=19,0	360	362
105	2,3-dihydroxybenzylamino	4-chlorobutyl	C=55,2; H=5,1; N=20,4	346	348
106	2,4-dihydroxybenzylamino	4-chlorobutyl	C=55,1; H=5,2; N=20,6	346	348
107	2,5-dihydroxybenzylamino	4-chlorobutyl	C=55,2; H=5,2; N=20,4	346	348
108	2,6-dihydroxybenzylamino	4-chlorobutyl	C=55,1; H=5,1; N=20,4	346	348
109	3,4-dihydroxybenzylamino	4-chlorobutyl	C=55,0; H=5,2; N=20,1	346	348
110	3,5-dihydroxybenzylamino	4-chlorobutyl	C=55,3; H=5,2; N=20,2	346	348
111	4-hydroxy-3,5-dimethoxybenzylamino	4-chlorobutyl	C=55,0; H=5,7; N=18,1	390	392
112	4-hydroxyl-2,6-dimethoxybenzylamino	4-chlorobutyl	C=55,1; H=5,7; N=18,2	390	392
113	4-hydroxy-3-methoxybenzylamino	4-chlorobutyl	C=56,1; H=5,6; N=19,6	360	362
114	3-hydroxy-4-methoxybenzylamino	4-chlorobutyl	C=56,1; H=5,5; N=19,7	360	362
115	2,3,4-trihydroxybenzylamino	4-chlorobutyl,	C=52,1; H=4,7; N=19,8	362	364
116	2,4,5-trihydroxybenzylamino	4-chlorobutyl	C=52,4; H=4,9; N=19,5	362	364
117	2-hydroxy-3-methylbenzylamino	4-chlorobutyl	C=58,7; H=5,7; N=20,7	344	346
118	2-hydroxy-5-methylbenzylamino	4-chlorobutyl	C=59,2; H=5,9; N=19,9	344	346
119	4-hydroxy-3-methylbenzylamino	4-chlorobutyl	C=58,7; H=5,8; N=20,4	344	346
120	4-hydroxy-5-methylbenzylamino	4-chlorobutyl	C=58,9; H=5,7; N=20,4	344	346
121	3-hydroxyfurfurylamino	4-chlorobutyl	C=52,2; N=5,0; N=22,4	320	322
122	4-hydroxyfurfurylamino	4-chlorobutyl	C=52,1; H=5,0; N=22,1	320	322
123	5-hydroxyfurfurylamino	4-chlorobutyl	C=52,4; H=5,2; N=21,9	320	322
124	2-hydroxyanilino	4-chlorobutyl	C=56,7; H=5,1; N=21,9	316	318
125	3-hydroxyanilino	4-chlorobutyl	C=56,3; H=5,0; N=22,3	316	318

(continued)

PURINE SUBSTITUENT			CHN ANALYSES [%]	MS ANALYSES - ZMD	
	R6	R9		[M-H]$^{-*}$ a)	[M+H]$^{+*}$ b)
126	4-hydroxyanilino	4-chlorobutyl	C=56,6; H=5,0; N=22.4	316	318

a) solution: MeOH p.a. + HCOOH
b) solution: MeOH p.a. + H_2O + NH_3
* for Cl^{35}

[0048] EXAMPLE 13: 6-(4-hydroxybenzylamine)-9-(1-ethoxyeth-2-yl)purine. A mixture of 10 mmol (2270 mg) of 6-chloro-9-(1-ethoxyeth-2-yl)purine made of 10 mmol (1546 mg) of 6-chloropurine, 12 mmol (1478 mg) of 4-hydroxybenzylamine, and 4 mL of N-ethyldiisopropylamine was refluxed in n-butanol for 3 hrs. After removal of the *n*-butanol by vacuum evaporation, the resulting material was treated with water and extracted into ethyl acetate. The ethyl acetate phase was evaporated and the residuum subsequently washed with 30 ml of hexane. The solid residue was filtered off and the crude product crystallized from isopropanol. Yield: 65 %, white solid. TLC ($CHCl_3$:CH_3OH:NH_3 (85:15:0.1) (v:v): single spot; HPLC: purity > 98 %. ^{1}H NMR (400 MHZ, DMSO): 1.12t(3H, J = 6.8 Hz); 3.16m(1H); 3.23m(1 H); 3.82dd (2H, J_a = 13.0 Hz, J_b = 3.8 Hz); 4.31 m (2H); 4.60s(2H); 6.70d(2H, J = 8.3 Hz); 7.30d(2H, J =8.3 Hz); 8.18bs(1H); 8.23s (1H); 8.32s(1H); 9.25s(1 H). MS (ES): $[M+H]^+$= 314 (100).

Table 4: Compounds prepared by the method of example 13

PURINE SUBSTITUENT			CHN ANALYSES [%]	MS ANALYSES-ZMD	
	R6	R9		[M-H]$^{-*}$ a)	[M+H]$^{+*}$ b)
127	(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	1-ethoxyeth-2-yl	C=57,0; H=7,2; N=24,3	290	292
128	(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	1-ethoxyeth-2-yl	C=57,1; H=7,3; N=24,2	290	292
129	4-hydroxy-3-methylbutylamino	1-ethoxyeth-2-yl	C=57,1; H=7,6; N=24.2	292	294
130	4-hydroxybut-2-en-1-ylamino	1-ethoxyeth-2-yl	C=56,3; H=6,9; N=25.2	276	278
131	2-hydroxybenzylamino	1-ethoxyeth-2-yl	C=60,9; H=6,0; N=22,9	312	314
132	3-hydroxybenzylamino	1-ethoxyeth-2-yl	C=61,1; H=6,0; N=22,5	312	314
133	4-hydroxybenzylamino	1-ethoxyeth-2-yl	C=60,8; H=6,1; N=22,5	312	314
134	2-hydroxy-3-methoxybenzylamino	1-ethoxyeth-2-yl	C=59,1; H=6,0; N=21.0	342	344
135	2-hydroxy-4-methoxybenzylamino	1-ethoxyeth-2-yl	C=59,5; H=6,0; N=20,6	342	344
136	2-hydroxy-5-methoxybenzylamino	1-ethoxyeth-2-yl	C=59,3; H=6,0; N=20,9	342	344
137	2,3-dihydroxybenzylamino	1-ethoxyeth-2-yl	C=58,0; H=5,7; N=21,4	328	330
138	2,4-dihydroxybenzylamino	1-ethoxyeth-2-yl	C=58,5; H=5,5; N=21,9	328	330
139	2,5-dihydroxybenzylamino	1-ethoxyeth-2-yl	C=58,4; H=5,8; N=21,3	328	330
140	2,6-dihydroxybenzylamino	1-ethoxyeth-2-yl	C=58,5; H=5,8; N=21,7	328	330
141	3,4-dihydroxybenzylamino	1-ethoxyeth-2-yl	C=58,1; H=5,7; N=21,7	328	330
142	3,5-dihydroxybenzylamino	1-ethoxyeth-2-yl	C=58,3; H=5,8; N=21,8	328	330
143	4-hydroxyl-3,5-dimethoxybenzylamino	1-ethoxyeth-2-yl	C=57,4; H=6,4; N=19,0	372	374
144	4-hydroxyl-2,6-dimethoxybenzylamino	1-ethoxyeth-2-yl	C=57,6; H=6,8; N=19,3	372	374
145	4-hydroxy-3-methoxybenzylamino	1-ethoxyeth-2-yl	C=59,2; H=6,2; N=20.4	342	344
146	3-hydroxy-4-methoxybenzylamino	1-ethoxyeth-2-yl	C=59,0; H=6,3; N=20,4	342	344

(continued)

	PURINE SUBSTITUENT		CHN ANALYSES [%]	MS ANALYSES-ZMD	
	R6	R9		[M-H]$^{-*}$ a)	[M+H]$^{+*}$ b)
147	2,3,4-trihydroxybenzylamino	1-ethoxyeth-2-yl	C=55,5; H=5,6; N=20,8	344	346
148	2,4,5-trihydroxybenzylamino	1-ethoxyeth-2-yl	C=55,1; H=5,3; N=20,4	344	346

a) solution: MeOH p.a. + HCOOH
b) solution: MeOH p.a. + H_2O + NH_3
* for Cl^{35}

[0049] EXAMPLE 14: Estimation of cytokinin biological activity of novel compounds in callus bioassay. Cytokinin-dependent tobacco callus *Nicotiana tabacum* L. cv. Wisconsin 38 was maintained at 25°C in darkness on modified MS medium, containing per 1 liter: 4 mmol of nicotinic acid, 2.4 mmol of pyridoxine hydrochloride, 1.2 mmol of thiamine, 26.6 mmol of glycine, 1.37 mmol of glutamine, 1.8 mmol of myo-inositol, 30 g of sucrose, 8 g of agar, 5.37 mmol of NAA, and 0.5 mmol of the compound tested. Subcultivation was carried out every three weeks. Fourteen days before the bioassay, the callus tissue was transferred to the media without the compound tested. The biological activity was determined from the increase of the fresh callus weight after four weeks of cultivation. Five replicates were prepared for each concentration of the compound tested and the entire test was repeated twice. From the obtained data, the concentration with the highest activity was selected for each compound tested. The relative activity of the compound at this concentration was calculated (Table 8). The activity obtained for 10^{-5} M 6-benzylaminopurine (BAP) was defined as 100 %.

[0050] The compounds to be tested were dissolved in dimethylsulfoxide (DMSO) and the solution brought up to 10^{-3} M with distilled water. This stock solution was further diluted with the respective media used for the biotest to a concentration ranging from 10^{-8} M to 10^{-4} M. The final concentration of DMSO did not exceed 0.2 % and therefore did not affect the biological activity in the assay system used. The compounds listed in Table 5 can be divided into two groups. The first group contains natural cytokinins represented by N^6-substituted purines (compounds known in the prior art serving as control). The second group contains the novel 6,9-disubstituted purines derived from the compounds of the first group. The results in Table 5 show that the substitution in position 9 of the purine ring by tetrahydropyranyl, tetrahydrofuranyl and other easily cleavable substituents generally led to an increase of the cytokinin activity in the callus bioassay in comparison to the original cytokinin analogues.

Table 5: The effect of novel compounds on the growth of cytokinin-dependent tobacco callus *Nicotiana tabacum* L. cv. Wisconsin 38

Tested compound		**concentration with highest activity (mol.l^{-1})**	**activity (%) [10^{-5}mol.l^{-1} BAP = 100%]**
R6	**R9**		
benzylamino	H	10^{-6}	100
benzylamino	tetrahydropyran-2-yl	10^{-6}	103 (± 12)
2-hydroxybenzylamino	H	10^{-6}	72.3 (± 9)
2-hydroxybenzylamino	tetrahydropyran-2-yl	10^{-5}	80 (± 7)
2-hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-5}	78 (± 8)
3-hydroxybenzylamino	H	10^{-5}	116 (± 11)
3-hydroxybenzylamino	tetrahydropyran-2-yl	10^{-5}	139 (± 16)
3-hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-5}	125 (± 14)
3-hydroxybenzylamino	4-chlorobutyl	10^{-4}	111.6 (± 20)
3-hydroxybenzylamino	1-ethoxyethyl	10^{-4}	109.4 (± 14)
4-hydroxybenzylamino	H		n.a.
4- hydroxybenzylamino	tetrahydropyran-2-yl	10^{-5}	36 (± 5)
4-hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-5}	27 (± 6)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	H	10^{-5}	869 (± 12)

(continued)

Tested compound		concentration with highest activity (mol.l^{-1})	activity (%) [10^{-5}mol.l^{-1} BAP = 100%]
R6	R9		
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	10^{-5}	965 (± 3)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	10^{-5}	89 (± 12)
(E)-4-hydroxy-3-methylbut-2-en-1-ylamino)	4-chlorobutyl	10^{-4}	103.5 (± 16)
(E)-4-hydroxy-3-methylbut-2-en-1-ylamino)	1-ethoxyethyl	10^{-4}	102.8 (± 15)
4-hydroxy-3-methylbutylamino	H	10^{-5}	83.2 (± 15)
4-hydroxy-3-methylbutylamino	tetrahydropyran-2-yl	10^{-5}	112 (± 13)
4-hydroxy-3-methylbutylamino	tetrahydrofuran-2-yl	10^{-5}	105 (± 11)
4-hydroxy-3-methylbutylamino	4-chlorobutyl	10^{-4}	84 (± 8)
4-hydroxy-3-methylbutylamino	1-ethoxyethyl	10^{-4}	95 (± 6)
2-hydroxy-3-methoxybenzylamino*	H		n.a.
2-hydroxy-3-methoxybenzylamino	tetrahydropyan-2-yl	10^{-6}	11 (± 1)
3,5-dihydroxybenzylamino*	H	10^{-6}	39 (± 6)
3,5-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-6}	45 (± 4)
2-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	10^{-6}	43 (± 2)
2,4-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-5}	5 (± 4)
2,5-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-5}	20 (± 8)
3,4-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-5}	61 (± 13)
4-hydroxy-3,5-dimethoxybenzylamino	tetrahydropyran-2-yl	10^{-5}	39 (± 12)
4-hydroxy-2,6-dimethoxybenzylamino	tetrahydropyran-2-yl	10^{-5}	43 (± 15)
4-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	10^{-6}	62 (± 8)
3-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	10^{-6}	55 (± 17)
2-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	10^{-5}	9.2 (± 7)
2-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	121 (± 11)
4-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	10^{-5}	4 (± 3)

(continued)

Tested compound		concentration with highest activity (mol.l^{-1})	activity (%) [10^{-5}mol.l^{-1} BAP = 100%]
R6	R9		
4-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	10^{-5}	6 (± 2)
3-hydroxyfurfurylamino	tetrahydropyran-2-yl	10^{-6}	52 (± 17)
4-hydroxyfurrurylamino	tetrahydropyran-2-yl	10^{-6}	91 (± 13)
2-hydroxyanilino	tetrahydropyran-2-yl	10^{-5}	30 (± 9)
3-hydroxyanilino	tetrahydropyran-2-yl	10^{-5}	65 (± 13)
4-hydroxyanilino	tetrahydropyran-2-yl	10^{-5}	22 (± 6)
4-hydroxy-3-methylanilino	tehahydropyran-2-yl	10^{-5}	12 (± 4)
4-hydroxy-5-methylanilino	tetrahydropyran-2-yl	10^{-5}	10 (± 7)
4-hydroxy-3,5-dimethoxyanilino	tetrahydropyran-2-yl	10^{-5}	19 (± 9)
4-hydroxy-2,6-dimethoxyanilino	tetrahydropyran-2-yl	10^{-5}	15 (± 11)
4-hydroxy-3,5-dimethoxybenzylamino	tetrahydrofuran-2-yl	10^{-6}	27 (± 9)
4-hydroxy-2,6-dimethoxybenzylamino	tetrahydrofuran-2-yl	10^{-5}	31 (± 7)
3-hydroxy-4-methoxybenzylamino	tetrahydrofuran-2-yl	10^{-6}	47 (± 12)
4-hydroxy-3-methylbenzylamino	tetrahydrofuran-2-yl	10^{-5}	12 (± 3)
4-hydroxy-5-methylbenzylamino	tetrahydrofuran2-yl	10^{-5}	2 (± 0.8)
4-hydroxyanilino	tetrahydrofuran-2-yl	10^{-5}	10 (± 3)
4-hydroxy-3-methylanilino	tetrahydrofuran-2-yl	10^{-5}	7 (± 2)
n. a. means not active *the control cytokinin described in Doležal et al. (Bioorg. Med.Chem. 14: 875, 2006).			

[0051] EXAMPLE 15: Testing of novel compounds for typical cytokinin activity in *Amaranthus* bioassay. A standard *Amaranthus* bioassay was performed with several modifications. The seeds of *Amaranthus caudatus* var. *atropurpurea* were surface-sterilized in 10% (w/v) N-chlorobenzenesulfonamide for 10 min and washed 5 times with deionized water. They were placed in 14 cm Petri dishes containing paper tissues saturated with deionized water. After 72 h of cultivation at 25°C in darkness, the roots of the seedlings were cut off. The explants, consisting of two cotyledons and hypocotyls, were placed in 5 cm Petri dishes onto two layers of filter paper soaked with 1 ml of the incubation medium containing 10 mmol of NA_2HPO_4-KH_2PO_4, pH 6.8, 5 mmol of tyrosine and the compound to be tested. There were 20 explants per dish. The procedure was carried out under a green safe light in a darkroom. After 48 h of incubation at 25°C in darkness, betacyanin was extracted by freezing the explants in 4 ml 3.33 mM acetic acid. The concentration of betacyanin was determined from the absorbencies at 537 nm and 620 nm as follows: $DA = A_{537nm} - A_{620nm}$. From the obtained data, the concentration with the highest activity was selected for each compound tested. Relative activity of the compound at this concentration was calculated. The activity obtained for 10^{-5} M 6-benzylaminopurine (BAP) was defined as 100 %. The values shown in Table 6 are means of five replicates and the entire test was repeated twice.

[0052] The compounds to be tested were dissolved in dimethylsulfoxide (DMSO) and the solution brought up to 10^{-3} M with distilled water. This stock solution was further diluted with the respective media used for the biotest to a concentration ranging from 10^{-8}M to 10^{-4}M. The final concentration of DMSO did not exceed 0.2 % and therefore did not affect the biological activity in the assay system used. The compounds listed in Table 6 can be again divided into two groups.

The first group contains classical cytokinin represented by N^6-substituted purines (compounds known in the prior art serving as control). The second group contains the novel 6,9-disubstituted derivatives of the compounds of the first group. The results show that the substitution in position 9 of the purine skeleton generally led to an increase of betacyanin (purple color) content in *Amaranthus caudatus* cotyledon/hypocotyl explants in comparison to the corresponding natural cytokinins.

Table 6: The effect of novel compounds on the betacyanin content in *Amaranthus caudatus* cotyledon/hypocotyl explants

Tested compound		Concentration with highest activity (mol.l^{-1})	Activity (%) [10^{-6}mol.l^{-1} BAP = 100%]
R6	R9		
benzylamino	H	10^{-5}	100
benzylamino	tetrahydropyran-2-yl	10^{-4}	120.7 (± 18)
2-hydroxybenzylamino	H	10^{-4}	32.6 (± 12)
2-hydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	41.6 (± 5)
2-hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	33 (± 5)
2-hydroxybenzylamino	4-chlorobutyl	10^{-4}	47.5 (± 8)
3-hydroxybenzylamino	H	10^{-5}	99 (± 15)
3-hydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	105.1 (± 21)
3-hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	107 (± 16)
3-hydroxybenzylamino	4-chlorobutyl	10^{-4}	102.5 (± 18)
3-hydroxybenzylamino	1-ethoxyethyl	10^{-4}	108.2 (± 18)
4-hydroxybenzylamino	H		n.a.
4- hydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	25.3 (± 9)
4- hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	13 (± 4)
4- hydroxybenzylamino	4-chlorobutyl	10^{-4}	33.4 (± 6)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	H	10^{-5}	116 (± 13)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	10^{-4}	299.4 (± 14)
(E)-(4-hydroy-3-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	10^{-4}	117 (± 7)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	4-chlorobutyl	10^{-4}	123.8 (± 12)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	1-ethoxyethyl	10^{-4}	92.5 (± 10)
4-hydroxy-3-methylbutylamino	H	10^{-4}	75 (± 13)
4-hydroxy-3-methylbutylamino	tetrahydropyran-2-yl	10^{-4}	83 (± 6)
4-hydroxy-3-methylbutylamino	tetrahydrofuran-2-yl	10^{-4}	80 (± 7)
4-hydroxy-3-methylbutylamino	4-chlorobutyl	10^{-4}	81 (± 6)
4-hydroxy-3-methylbutylamino	1-ethoxyethyl	10^{-4}	85 (± 7)

(continued)

Tested compound		Concentration with highest activity (mol.l^{-1})	Activity (%) [10^{-6}mol.l^{-1} BAP = 100%]
R6	R9		
2-hydroxy-3-mehoxybenzylamino	H	10^{-4}	19 (± 3)
2-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	32 (± 7)
2-hydroxy-3-methoxybenzylamino	4-chlorobutyl	10^{-4}	53 (± 6)
3,5-dihydroxybenzylamino*	H	10^{-5}	53 (± 9)
3,5-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-5}	53 (± 9)
2-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	37 (± 6)
2,5-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	35.1 (± 9)
3,4-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	52 (± 13)
4-hydroxy-3,5-dimethoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	8 (± 3)
4-hydroxy-2,6-dimethoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	12 (± 5)
4-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	57 (± 11)
3-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	41 (± 7)
2-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	68.8 (± 17)
2-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	68.4 (± 11)
4-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	7 (± 1)
4-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	5 (± 3)
3-hydroxyfurfurylamino	tetrahydropyran-2-yl	10^{-4}	65 (± 12)
4-hydroxyfurfurylamino	tetrahydropyran-2-yl	10^{-4}	115 (± 18)
2-hydroxyanilino	tetrahydropyran-2-yl	10^{-4}	65 (± 10)
3-hydroxyanilino	tetrahydropyran-2-yl	10^{-4}	122 (± 11)
4-hydroxyanilino	tetrahydropyran-2-yl	10^{-4}	32 (± 7)
4-hydroxy-3-methylanilino	tetrahydropyran-2-yl	10^{-4}	15 (± 5)
4-hydroxy-5-methylanilino	tetrahydropyran-2-yl	10^{-4}	17 (± 6)
4-hydroxy-3,5-dimethoxyanilino	tetrahydropyran-2-yl	10^{-4}	10 (± 4)
4-hydroxy-2,6-dimethoxyanilino	tetrahydropyran-2-yl	10^{-4}	8 (± 2)
4-hydroxy-3,5-dimethoxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	2 (± 1)

(continued)

Tested compound		Concentration with highest activity (mol.l^{-1})	Activity (%) [10^{-6}mol.l^{-1} BAP = 100%]
R6	R9		
4-hydroxy-2,6-dimethoxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	7 (± 3)
3-hydroxy-4-methoxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	32 (± 9)
4-hydroxy-3-methylbenzylamino	tetrahydrofuran-2-yl	10^{-4}	2 (± 0,7)
4-hydroxy-5-methylbenzylamino	tetrahydrofuran-2-yl	10^{-4}	22 (± 6)
4-hydroxyanilino	tetrahydrofuran-2-yl	10^{-4}	22 (± 6)
4-hydroxy-3-methylanilino	tetrahydrofuran-2-yl	10^{-4}	6 (± 3)
n. a. means not active *the control cytokinin described in Doležal et al. (Bioorg. Med.Chem. 14: 875, 2006).			

[0053] EXAMPLE 16: Testing of antisenescence properties of novel cytokinin compounds on wheat leaf segments. Seeds of winter wheat, *Triticum aestivum* cv. Hereward, were washed under running water for 24 hours and then sown on vermiculite soaked with the Knop's solution. They were placed in the grow chamber at 25°C with a 16h - 8 h light period at 50 mmol.m^{-2}.s^{-1}. After 7 days, the first leaf was fully developed and the second leaf had started to grow. A 35 mm long tip section of the first leaf, was removed from each of 5 seedlings and trimmed slightly to a combined weight of 100 mg. The basal ends of the five leaf tips were placed in the wells of a microtiter polystyrene plate containing 150 ml of the solution of the tested compound each. The entire plate was inserted into a plastic box lined with paper tissues soaked with distilled water to prevent leaf sections from drying out. After 96 h incubation in the dark at 25°C, the leaves were removed and chlorophyll was extracted by heating at 80°C for 10 min in 5 ml of 80 % ethanol (v/v). The sample volume was then restored to 5 ml by the addition of 80 % ethanol (v/v). The absorbance of the extract was recorded at 665 nm. In addition, chlorophyll extracts from fresh leaves and leaf tips incubated in deionized water were measured. From the obtained data, the concentration with the highest activity was selected for each compound tested. Relative activity of the compound at this concentration was calculated (Table 7). The activity obtained for 10^{-4} M 6-benzylaminopurine (BAP) was defined as 100%. The values shown are means of five replicates and the whole experiment was repeated twice.

[0054] The compounds to be tested were dissolved in dimethylsulfoxide (DMSO) and the solution brought up to 10^{-3} M with distilled water. This stock solution was further diluted with distilled water to a concentration ranging from 10^{-8} M to 10^{-4} M. The final concentration of DMSO did not exceed 0.2 % and therefore did not affect the biological activity in the assay system used.

[0055] The compounds listed in Table 7 can be divided into 2 groups. The first group contains natural cytokinins, represented by N^6-substituted purines (compounds known in the prior art serving as controls). The second group contains the novel 6,9-disubstituted purines derived from the compounds of the first group. The results show that the substitution in position 9 of the purine skeleton generally led to an increase of the antisenescent activity in comparison to the corresponding classical cytokinins.

Table 7: The effect of novel compounds on the retention of chlorophyll in excised wheat leaf tips (standard deviations of the mean for 10 replicate determinations are shown)

Tested compound		concentration with highest activity (mol.l^{-1})	activity (%) [10^{-4}mol.l^{-1} BAP = 100%]
R6	R9		
benzylamino	H	10^{-4}	100
benzylamino	tetrahydropyran-2-yl	10^{-4}	105 (± 0.5)
2-hydroxybenzylamino	H	10^{-4}	22.4 (± 5)
2-hydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	23.6 (± 7)
2-hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	26 (± 2)

(continued)

Tested compound		concentration with highest activity (mol.l^{-1})	activity (%) [10^{-4}mol.l^{-1} BAP = 100%]
R6	R9		
2-hydroxybenzylamino	4-chlorobutyl	10^{-4}	47.5 (± 8)
3-hydroxybenzylamino	H	10^{-4}	105.9 (± 14)
3-hydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	133.1 (± 15)
3-hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	113 (± 18)
3-hydroxybenzylamino	4-chlorobutyl	10^{-4}	102.5 (± 18)
3-hydroxybenzylamino	1-ethoxyethyl	10^{-4}	108.2 (t 18)
4-hydroxybenzylamino	H		n.a.
4- hydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	10.1 (± 9)
4- hydroxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	3 (± 1)
4- hydroxybenzylamino	4-chlorobutyl	10^{-4}	33.4 (± 8)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	H	10^{-4}	28.3 (± 17)
(E)-(4-hydroxy-3-methylbyt-2-en-1-ylamino)	tetrahydropyran-2-yl	10^{-4}	38.2 (± 7)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	10^{-4}	45 (± 6)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	4-chlorobutyl	10^{-4}	73.8 (± 12)
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	1-ethoxyethyl	10^{-4}	92.5 (± 10)
4-hydroxy-3-methylbutylamino	H	10^{-4}	89 (± 11)
4-hydroxy-3-methylbutylamino	tetrahydropyran-2-yl	10^{-4}	95 (± 8)
4-hydroxy-3-methylbutylamino	tetrahydrofuran-2-yl	10^{-4}	91 (± 4)
4-hydroxy-3-methylbutylamino	4-chlorobutyl	10^{-4}	89 (± 7)
4-hydroxy-3-methylbutylamino	1-ethoxyethyl	10^{-4}	94 (± 10)
2-hydroxy-3-methoxybenzylamino*	H	10^{-4}	34 (± 5)
2-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	50 (± 5)
3,5-dihydroxybenzylamino*	H	10^{-4}	134 (± 10)
3,5-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	145 (± 12)

(continued)

Tested compound		concentration with highest activity (mol.l^{-1})	activity (%) [10^{-4}mol.l^{-1} BAP = 100%]
R6	R9		
2-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	35 (± 9.5)
2,5-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	15 (± 5)
3,4-dihydroxybenzylamino	tetrahydropyran-2-yl	10^{-4}	71.3 (± 17)
4-hydroxy-3,5-dimethoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	42 (± 13)
4-hydroxy-2,6-dimethoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	22 (± 4)
4-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	55 (± 18)
3-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	10^{-4}	47 (± 11)
2-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	16.4 (± 3)
2-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	82 (± 12)
4-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	9 (± 2)
4-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	10^{-4}	3 (± 1)
3-hydroxyfurfurylamino	tetrahydropyran-2-yl	10^{-4}	45 (± 13)
4-hydroxyfurfurylamino	tetrahydropyran-2-yl	10^{-4}	101 (± 17)
2-hydroxyanilino	tetrahydropyran-2-yl	10^{-4}	11 (± 4)
3-hydroxyanilino	tetrahydropyran-2-yl	10^{-4}	23 (± 7)
4-hydroxy-3-methylanilino	tetrahydropyran-2-yl	10^{-4}	7 (± 5)
4-hydroxy-5-methylanilino	tetrahydropyran-2-yl	10^{-4}	10 (± 3)
4-hydroxy-3,5-dimethoxyanilino	tetrahydropyran-2-yl	10^{-4}	28 (± 9)
4-hydroxy-2,6-dimethoxyanilino	tetrahydropyran-2-yl	10^{-4}	14 (± 4)
4-hydroxy-3,5-dimethoxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	36 (± 10)
4-hydroxy-2,6-dimethoxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	14 (± 5)
3-hydroxy-4-methoxybenzylamino	tetrahydrofuran-2-yl	10^{-4}	35 (± 8)
4-hydroxy-3-methylbenzylamino	tetrahydrofuran-2-yl	10^{-4}	1,4 (± 2)

(continued)

Tested compound		concentration with highest activity (mol.l^{-1})	activity (%) [10^{-4}mol.l^{-1} BAP = 100%]
R6	R9		
4-hydroxy-5-methylbenzylamino	tetrahydrofuran-2-yl	10^{-4}	17 (± 5)
4-hydroxyanilino	tetrahydrofuran-2-yl	10^{-4}	28 (± 4)
4-hydroxy-3-methylanilino	tetrahydrofuran -2-yl	10^{-4}	4 (± 3)
*the control cytokinins described in Doležal et al. (Bioorg. Med.Chem. 14: 875, 2006).			

[0056] EXAMPLE 17: inhibition of aging of normal human cells by novel compounds. In this example, human diploid fibroblasts (HCA cells of various passage levels: passage 20 - designated HCA20; passage 40 - designated HCA40; passage 60 - designated HCA60) were stained for (3-galactosidase activity. The medium used for the cell cultivation was removed, the cells were washed twice in PNS, and fixed in 2-3 ml of fixing solution comprised of a 2% formaldehyde and 0.2% glutaraldehyde in PBS. The cells were incubated at room temperature for 5 minutes, and then washed twice with PBS. The cells were subsequently Incubated at 37°C (without CO_2) for 16 hours in 2-3 ml of the solution comprising potassium ferricyanide (5 mM), potassium ferrocyanide (5 mM), $MgCl_2$ (2 mM), X-gal (5-bromo-4-chloro-3-indolyl-β-D-galactopyranoside) (1 mg/ml), in citric/phosphate buffer, pH 6.0) Following this incubation period, the cell samples were observed in order to detect the presence of blue cells, indicating that X-gal had been cleaved (positively senescent cells). In this experiment, senescent cells, but no other cells were stained blue due to the action of β-galactosidase on the substrate.

Table 8: The effect of novel compounds on the number of senescent cells in the culture of human fibroblasts

Substituent		SENESCENT CELLS (%)		
R6	R9	HCA20	HCA40	HCA60
benzylamino	tetrahydropyran-2-yl	3	4	47
(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	4	5	15
4-hydroxy-3-methylbutylamino	tetrahydropyran-2-yl	5	2	25
2-hydroxybenzylamino	tetrahydropyran-2-yl	4	2	26
3-hydroxybenzylamino	tetrahydropyran-2-yl	5	3	25
4-hydroxybenzylamino	tatrahydropyran-2-yl	5	5	16
2-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	3	3	25
2-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	3	4	27
3,4-dihydroxybenzylamino	tetrahydropyran-2-yl	3	4	15
4-hydroxy-3,5-dimethoxybenzylamino	tetrahydropyran-2-yl	4	5	17
4-hydroxy-2,6-dimethobenzylamino	tetrahydropyran-2-yl	4	5	21
4-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	4	4	19
3-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	5	7	29
2-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	4	6	30
2-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	5	4	30
4-hydroxy-3-methylbenzylamino	tetrehydropyran-2-yl	4	6	22
4-hydroxy-5-methylbenzylamino	tetrahydropyran-2-y1	3	4	20
3-hydroxyfurfurylamino	tetrahydropyran-2-yl	4	4	18
4-hydroxyfurfurylamino	tetrahydropyran-2-yl	4	4	16
5-hydroxyfurfurylamino	tetrahydropyran-2-yl	4	7	24

(continued)

Substituent		SENESCENT CELLS (%)		
R6	R9	HCA20	HCA40	HCA60
2-hydroxyanilino	tetrahydropyran-2-yl	4	6	29
3-hydroxyanilino	tetrahydropyran-2-yl	5	4	28
4-hydroxyanilino	tetrahydropyran-2-yl	4	6	16
4-hydroxy-3-methylanilino	tetrahydropyran-2-yl	3	4	19
4-hydroxy-6-methylanilino	tetrahydropyran-2-yl	4	4	18
4-hydroxy-3,5-dimethoxyanilino	tetrahydropyran-2-yl	4	5	22
4-hydroxy-2,6-dimethoxyanilino	tetrahydropyran-2-yl	4	6	24
3-hydroxy-4-methoxyanilino	tetrahydropyran-2-yl	5	4	28
(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	4	5	15
4-hydroxy-3-methylbutylamino	tetrahydrofuran-2-yl	5	2	25
2-hydroxybenzylamino	tetrahydrofuran-2-yl	4	2	26
3-hydroxybenzylamino	tetrahydrofuran-2-yl	5	3	25
4-hydroxybenzylamino	tetrahydrofuran-2-yl	5	5	16

[0057] As shown in Table 8, with an increasing number of passages, the staining became darker. For the oldest cells, there were only blue cells ranging from bright blue to almost opaque color. 6,9-Disubstituted purine derivatives were very effective in comparison to 6-(benzylamino)-9-(tetrahydropyran-2-yl)purine in retaining much lower level of senescent cells after 60 passages. In the case of long-standing cultivation the cells treated with the compounds of the invention were able to live for a 30 % longer period than the control cells.

[0058] EXAMPLE 18: *In vitro* cytotoxic activity of novel compounds. Low cytotoxicity of the compounds is the major property determining their cosmetic use. One of the parameters used, as the basis for cytotoxicity assays, is the metabolic activity of viable cells. For example, a microtiter assay, which uses the Calcein AM, is now widely used to quantify cell proliferation and cytotoxicity. For Instance, this assay is used in drug screening programs and in chemosensitivity testing. Because only metabolically active cells cleave Calcein AM, these assays detect viable cells exclusively. The quantity of reduced Calcein AM corresponds to the number of vital cells in the culture.

[0059] Human T-lymphoblastic leukemia cell line CEM; promyelocytic HL-60 and monocytic U937 leukemias; breast carcinoma cell lines MCF-7, BT549, MDA-MB-231; glioblastoma U87MG cells: cervical carcinoma cells HELA; sarcoma cells U2OS and Saos2; hepatocellular carcinoma HepG2; mouse fibroblasts NIH3T3; mouse immortalized bone marrow macrophages B2.4 and B10A.4; P388D1 and L1210 leukemia; B16 and B16F10 melanomas; human osteosarcoma HOS; human myeloid leukemia K-562; human skin melanoma G-361 were used for routine screening of compounds. The cells were maintained in Nunc/Corning 80 cm^2 plastic tissue culture flasks and cultured in cell culture medium (DMEM with 5 g/l glucose, 2 mM glutamine, 100 U/ml penicillin, 100 mg/ml streptomycin, 10% fetal calf serum and sodium bicarbonate).

[0060] The cell suspensions that were prepared and diluted according to the particular cell type and the expected target cell density (2.500-30.000 cells per well based on cell growth characteristics) were added by pipette (80 ml) into 96-well microtiter plates. Inoculates were allowed a pre-incubation period of 24 hours at 37°C and 5% CO_2 for stabilization. Four-fold dilutions of the intended test concentration were added at time zero in 20 ml aliquots to the microtiter plate wells. Usually, the compound tested was evaluated at six 4-fold dilutions. In routine testing, the highest well concentration was 166.7 mM, but it can be changed depending on the agent. All drug concentrations were examined in duplicate. Incubations of cells with the tested compounds lasted for 72 hours at 37°C, in a 5% CO_2 atmosphere and 100% humidity. At the end of the incubation period, the cells were assayed by using Calcein AM. Ten microliters of the stock solution were pipetted into each well and incubated for 1 hour. Fluorescence (FD) was measured with the Labsystem FIA Reader Fluoroscan Ascent (UK). The tumor cell survival (GI_{50}) was calculated using the following calculation: TCS= ($FD_{drug\ exposed\ well}$/ mean $FD_{control\ wells}$) x 100%. The GI_{50} value, the drug concentration lethal to 50 % of the tumor cells, was calculated from the obtained dose response curves.

[0061] Zero cytotoxicity of the novel compounds is the basic prerequisite for cosmetic applications. The cytoxicity of the novel compounds was tested on a panel of cell lines of different histogenetic and species origin (Table 9). We show

herein that equal activities were found in all tumor cell lines tested, however, the non-malignant cells, e.g., NIH3T3 fibroblasts and normal human lymphocytes, were resistant to 6,9-disubstituted purine induced cytotoxicity. The compounds listed in Table 9 can be divided into 2 groups. The first group contains "classical cytokinins" represented by 6-substituted purines (which are known in the prior art). The second group contains the novel 6,9-disubstituted derivatives of these compounds. The results show that the substitution in position 9 of the purine skeleton by tetrahyropyranyl or tetrahydrofuranyl group generally led to a decrease in the cytotoxic activity in comparison to the "classical cytokinin" analogues. As demonstrated in Table 9, GI_{50} for NIH3T3 fibroblasts and normal human lymphocytes was always higher than 166.7 mM. The novel derivatives show no toxicity to normal and tumor cells in concentrations of about 166.7 mM and thus are more suitable for cosmetic applications than natural cytokinins (6-substituted purine derivatives) and the control substance 6-benzylamino-9-(tetrahydropyran-2-yl)purine.

Table 9: Cytotoxicity of novel compounds for different cancer cell lines

		Cell line tested / GI_{50} (μmol/L)					
R6	**R9**	**HOS**	**K-562**	**MCF7**	**NIH-3T3**	**CEM**	**HL60**
furfurylamino	H	>166.7	164.1	>166.7	>166.7	155.1	148.7
isopentenylamino	H	> 166.7	146.9	>166.7	>166.7	92.2	>166.7
benzylamino	H	> 166.7	138.9	166.1	> 166.7	>166.7	>166.7
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	H	>166.7	>166.7	>166.7	>166.7	>166.7	>166.7
3-hydroxybenzylamino	H	>166.7	128.4	>166.7	> 166.7	90.1	79.2
2-hydroxybenzylamino	H	>166.7	>166.7	>166.7	>166.T	69.2	78
benzylamino	tetrahydropyran-2-yl	>166.7	123.4	158.2	>166.7	>166.7	163.4
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydropyran-2-yl	>166.7		>166.7	>166.7	>166.7	>166.7
4-hydroxybenzylamino	tetrahydropyran-2-yl	>166.7		>166.7	>166.7	>166.7	>166.7
2-hydroxy-5-methoxybenzylamino	tetrahydropyran-2-yl	>166.7	>166.7	>166.7	>166.7	>166.7	>166.7
3-hydroxy-4-methoxybenzylamino	tatrahydropyran-2-yl	>166.7		>166.7	>166.7		>166.7
4-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	>116.7		>166.7	>160.7	>166.7	>166.7
4-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	>166.7		>166,7	>1667	>166.7	>1667
4-hydroxyfurfurylamino	tetrahydropyran-2-yl	>166.7	> 166.7	>166.7	>166.,7		>166.,7
4-hydroxy-3-methylanilino	tetrahydropyran-2-yl	>166.7		>166.7	>166.7		>166.7
4-hydroxy-5-methylanilino	tetrahydropyran-2-yl	>166.7		>166.7	>166.7		>166.7
2,4-dihydroxyanilino	tetrahydropyran-2-yl	> 166.7		>166.7	>166.7		>166.7
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	tetrahydrofuran-2-yl	>166.7		>166.7	>166.7		>166.7

(continued)

		Cell line tested / GI_{50} (μmol/L)					
R6	R9	HOS	K-562	MCF7	NIH-3T3	CEM	HL60
4-hydroxybenzylamino	tetrahydrofuran-2-yl	>166.7		>166.7	> 166.7		>166.7
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	4-chlorobutyl	>166.7		>166.7	>166.7		>166.7
4-hydroxybenzylamino	4-chlorobutyl	>166.7		>166.7	>166.7		> 166.7
(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)	1-ethoxyeth-2-yl	>166.7		>166.7	>166.7		>166.7
4-hydroxybenzylamino	1-ethoxyeth-2-yl	>166.7		>166.7	>166.7		>166.7

[0062] Example 19: Immunosuppressive activity. Compounds having the ability to selectively inhibit lymphocyte proliferation are potent immunosuppressants which can be also used with advantage in cosmetic applications. One of the most important parameters of specific cellular immunity is the proliferative response of lymphocytes to antigens or polyclonal mitogens. The majority of normal mammalian peripheral lymphocytes are resting cells. Antigens or nonspecific polyclonal mitogens have the capacity to activate lymphoid cells and this is accompanied by dramatic changes of intracellular metabolism (mitochondrial activity, protein synthesis, nucleic acids synthesis, formation of blastic cells and cellular proliferation). A variety of *in vitro* assays has been developed to measure the proliferative response of lymphocytes. The most commonly used one is the ^{3}H-thymidine incorporation method.

[0063] During the cell proliferation, DNA must to be replicated before the cell divides into two daughter cells. This dose association between cell doubling and DNA synthesis is very attractive for assessing the cell proliferation. If labeled DNA precursors are added to the cell culture, the cells that are about to divide incorporate the labeled nucleotide into their DNA. Traditionally, those assays usually involve the use of radiolabeled nucleosides, particularly tritiated thymidine ([^{3}H]-TdR). The amount of the [^{3}H]-TdR incorporated into the cellular DNA is quantified by liquid scintillation counting.

[0064] Human heparinized peripheral blood was obtained from healthy volunteers by cubital vein puncture. The blood was diluted in PBS (1:3) and mononuclear cells were separated by centrifugation In Ficoll-Hypaque density gradient (Pharmacia, 1.077 g/ml) at 2200 rpm for 30 minutes. Following centrifugation, lymphocytes were washed in PBS and resuspended in cell culture medium (RMPI 1640, 2 mM glutamine, 100 U/ml penicillin, 100 mg/ml streptomycin, 10 % fetal calf serum and sodium bicarbonate).

[0065] The cells, diluted at the target density of 1,100,000 cells/ml, were added by pipette (180 ml) into 96/well microtiter plates. Four-fold dilutions of the intended test concentration were added at time zero in 20 ml aliquots to the microtiter plate wells. Usually, the tested compound was evaluated at six sequential 4-fold dilutions. In routine testing, the highest well concentration was 266.7 mM. All drug concentrations were examined in duplicate. All wells with the exception of unstimulated controls were activated with 50 ml of concanavalin A (25 mg/ml). Incubations of cells with the tested compound lasted for 72 hours at 37°C, in 5% CO_2 atmosphere and 100% humidity. At the end of the incubation period, the cells were assayed by using the [^{3}H]-TdR.

[0066] Cell cultures were Incubated with 0.5 mCi (20 ml of stock solution 500 mCi/ml) per well for 6 hours at 37°C and 5% CO_2. The automated cell harvester was used to lyse the cells in water and adsorb the DNA onto glass-fiber filters in the form of microtiter plates. The DNA, incorporating [^{3}H]-TdR was retained on the filter while unincorporated material passed through. The filters were dried at room temperature overnight and sealed into a sample bag with 10-12 ml of scintillant. The amount of the [^{3}H]-TdR present in each filter (in cpm) was determined by scintillation counting in the Betaplate liquid scintillation counter. The effective dose of the immunosuppressant (ED) was calculated using the following equation: ED = ($CPM_{drug\ exposed\ well}$/ mean $CPM_{control\ wells}$) x 100 % (CPM = counts per minute). The ED_{50} value, the drug concentration inhibiting proliferation of 50 % of lymphocytes, was calculated from the obtained dose response curves.

[0067] To evaluate immunosuppressive activity of 6,9-disubstituted purines, their ability to inhibit polyclonal mitogen induced proliferation of normal human lymphocytes was analyzed (Table 10). Our data demonstrate that these compounds have only marginal activity on the ^{3}H-thymidine Incorporation, nonetheless, they efficiently inhibit proliferation of activated lymphocytes. The effective immunosuppressive dose of the novel derivatives under *in vitro* conditions was close to 1-20 mM. These results represent new discovery of biological activity of cytokinin derived compounds which might find an application in cosmetics.

Table 10: Immunosupressive activity of novel compounds.

Tested compound		Human lymphocytes ED_{50} (mM)
R6	**R9**	
benzylamino	H	n.a.
2-hydroxybenzylamino	H	68
3-methylbut-2-en-1-ylamino	H	79.5
benzylamino	tetrahydropyran-2-yl	44.7
2-hydroxybenzylamino	tetrahydropyran-2-yl	4.5
2-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	7
2-hydroxy-4-methoxybenzylamino	tetrahydropyran-2-yl	4.2
3,4-dihydroxybenzylamino	tetrahydropyran-2-yl	9.5
3,5-dihydroxybenzylamino	tetrahydropyran-2-yl	18.7
2-hydroxy-3-methylbenzylamino	tetrahydropyran-2-yl	2.2
2-hydroxy-5-methylbenzylamino	tetrahydropyran-2-yl	6.4
2-hydroxybenzylamino	tetrahydrofuran-2-yl	10.2
2-hydroxy-3,5-dimethoxybenzylamino	tetrahydrofuran-2-yl	6.5
2-hydroxy-4-methoxybenzylamino	tetrahydrofuran-2-yl	9.7
2-hydroxy-3-methylanilino	tetrahydrofuran-2-yl	14.3
2-hydroxybenzylamino	4-chlorobutyl	6.7
2-hydroxy-3-methoxybenzylamino	4-chlorobutyl	9.2
2-hydroxy-4-methoxybenzylamino	4-chlorobutyl	8.3
3,4-dihydroxybenzylamino	1-ethoxyethyl	10.8
3,5-dihydroxybenzylamino	1-ethoxyethyl	21.4
n. a. means not active		

[0068] EXAMPLE 20: Anti-inflammatory activity. The compounds of formula 1 having anti-inflammatory activities can be used as cosmetics for treating Inflammation skin disorders as atopic dermatitis, lichen planus, hyperpigmentation and Herpes simplex lesions. From this reason, rat C6 glioma (ATCC No. CCL107) was cultivated as a monolayer in a serum-free chemically defined medium containing Ham's F10-minimal essential medium (1:1 v/v), 2 mM L-glutamine, 1 % (v/v) minimal essential medium vitamins (100x), 1 % (v/v) minimal essential medium nonessential amino acids (100x), 100U/ml penicillin, 100 mg/ml streptomycin and 30 nM sodium selenite. Incubation was performed at 37°C in a humidified atmosphere. The assays were performed in the logarithmic growth phase at a density of $2.5x10^5$ cells/cm^2. Intracellular cAMP synthesis was induced by addition of 5 mM (-)isoproterenol. After 30 min incubation at 37°C the medium was removed and the cellular amount of cAMP was determined using the cAMP-enzyme immunoassay Amersham kit. The I_{50} value was determined from a dose-response curve in duplicate. The effect of the novel 6,9-disubstituted purines was measured after simultaneous addition with isoproterenol. The classical cytokinins, known in the prior art, were inactive.

Table 11: Modulation of the activity of β-adrenergic receptors by substituted purines

Tested compound		Effect
R6	R9	
benzylamino	H	n.a.
3-hydroxybenzylamino	H	n.a.
furfurylamino	H	n.a.

(continued)

Tested compound		Effect
R6	R9	
4-hydroxybenzylamino	tetrahydropyran-2-yl	1.8- fold activation
3,4-dihydroxybenzylamino	tetrahydropyran-2-yl	1.7-fold activation
4-hydroxy-2,6-dimethoxybenzylamino	tetrahydropyran-2-yl	1.3-fold activation
4-hydroxy-3-methoxybenzylamino	tetrahydropyran-2-yl	1.6-fold activation
n. a. means not active		

[0069] As $P2Y_1$-like and A2 purinergic receptors, negatively and positively coupled to adenylate cyclase, respectively, are present in rat C6 glioma, it remains to be determined whether the modulation of the synthesis of cAMP is due to the inhibition of the activation of β-adrenergic receptors by isoproterenol, or due to the activation of purinergic receptors.

[0070] EXAMPLE 21: Development and content of an ointment. An ointment formulation suitable for treating psoriatic skin disorders is described. The formulation components are given below (expressed in ingredient grams per 100 g ointment).

	Ingredient/100 g
6-(4-hydroxybenzyl)amino-9 -(tetrahydropyran-2-yl)purin (pTTHP)	1.0 g
butylhydroxytoluenum (Nipanox BHT)	0.2 g
butylparaben (Nipabutyl)	0.2 g
diethylene glycol monoethyl ether (Transcutol P)	10.0 g
glycerol dibehenate (Compritol 888 ATO)	22.0 g
propylene glycol laurate (Lauroglycol FCC)	66.6 g

[0071] The possible ointment consistency may be further modified by addition of vaselinum album. It is expected that the transdermal Transcutol P/Lauroglycol FCC system will increase the efficiency of pTTHP.

[0072] EXAMPLE 22: Gel formulation. A gel formulation suitable for treating psoriatic skin disorders is described. The formulation components are given below (expressed in ingredient grams per 100 g gel).

	Ingredient/100 g
6-(4-hydroxybenzyl)amino-9 -(tetrahydropyran-2-yl)purin (pTTHP)	1.0 g
butylhydroxytoluenum (Nipanox BHT)	0.2 g
butylparaben (Nipabutyl)	0.2 g
diethylene glycol monoethyl ether (Transcutol P)	10.0 g
silica colloidalis anhydrica (Zeopharm 177)	5.0 g
propylene glycol laurate (Lauroglycol FCC)	83.6 g

[0073] The gel consistency may be additionally modified by addition of silica colloidalis anhydrica. It is again expected that the transdermal Transcutol P/Lauroglycol FCC system will increase the efficiency of pTTHP. Silica colloidalis anhydrica is expected to slow down the penetration of the active substance.

[0074] EXAMPLE 23: Preparation procedure for an ointment to be applied topically to skin. Such an ointment formulation is as follows:

	Ingredient/200g
6-(4-hydroxybenzyl)amino-9 -(tetrahydropyran-2-yl)purin (pTTHP)	2.0 g
butylhydroxytoluenum (Nipanox BHT)	0.4 g
butylparaben (Nipabutyl)	0.4 g

(continued)

	Ingredient/200g
diethylene glycol monoethyl ether (Transcutol P)	20.0 g
glycerol dibehenale (Compritol 888 ATO)	44.0 g
propylene glycol laurate (Lauroglycol FCC)	133.2 g

Recommended procedure:

[0075] Phase A - pTTHP (2 g) was dissolved in 20 g of Transcutol P while stirring continuously at room temperature in a first container. The dissolution process may be accelerated by heating the solution to a maximum temperature of 40°C.

[0076] Phase B - Nipanox BHT(0.4 g) and 0.4 g of Nipabutyl were dissolved while stirring continuously in 133.2 g of Lauroglycol FCC at a temperature of approximately 70°C in a second container. The clear oily solution is heated to a temperature of approximately 80°C and 44 g of Compritol 888 ATO are melted in it while stirring continuously. The clear oily solution is cooled down to approximately 60°C.

[0077] As Phase B is cooled and with continuous stirring, Phase A is added. A whitish ointment-like substance is obtained and then filled into plastic containers (about 15 g ointment per container).

[0078] EXAMPLE 24: Formulation of a composition for topical application to the skin. A composition for topical application to the skin contains the following ingredients:

		Amount
6-(4-hydroxybenzyl)amino-9 -(tetrahydropyran-2-yl)purin (pTTHP)		0.1 %
Oil phase:		
	Cetyl alcohol	5.0 %
	Glyceryl monostearate	15.0 %
	Sorbitan monooleate	0.3 %
	Polysorbate 80 USP	0.3 %
Aqueous phase		
	Methylcellulose 100 cps	1.0 %
	Methyl paraben	0.25 %
	Propyl paraben	0.15 %
	Purified water	q.s. to 100 %

[0079] Methyl paraben and propyl paraben were dissolved in hot water and subsequently methylcellulose was dispersed in the hot water. The mixture was chilled at 6°C until the methylcellulose dissolved (aqueous phase). The aqueous phase was then heated to 72°C and added to the oil phase at 70°C while stirring continuously. pTHPP was added at a temperature of 35°C and the resulting mixture was stirred continuously until dispersion. This composition can be applied to the skin on at least a daily basis until the desired skin-ameliorating (anti-ageing) effect is reached.

[0080] EXAMPLE 25: Evaluation of Various Substituted Benzyl Pyranyl Aminopurines on Human Skin Fibroblasts. The following aminopurines were evaluated to determine their short term effect on human skin fibroblasts:

(1) 6-(2-hydroxybenzylamino)-9-tetrahydropyranylpurine;
(2) 6-(3-hydroxybenzylamino)-9-tetrahydropyranylpurine;
(3) 6-(2-methoxybenzylamino)-9-tetrahydropyranylpurine; and
(4) 6-(3-methoxybenzylamino)-9-tetrahydropyranylpurine.

[0081] Kinetin (N6-furfuryladenine) and/or 6-furfurylamino-9-tetrahydropyanylpuine were used as controls.

[0082] General Procedures. Stock solutions of the test compounds were prepared by dissolving about 40-60 mg in 1 ml DMSO. 250 μL of its volume was further diluted into 100 ml of complete medium. The maximum DMSO concentration in the medium was 0.25%; the final concentration of the substance in the medium was 400 μM. The stock solution was stored in fridge at 4°C. The stock solution was diluted in the cell culture medium (DMEM) as required.

[0083] All experiments were performed on early and nearing to late passage cultures of normal human adult skin

fibroblast line (cell line SNF20 established from a mammary skin biopsy obtained from a young, twenty year old, non-smoking and healthy female at the time of breast reduction operation). In order to check the effects of test compounds on senescent cells, late passage cells with 90% lifespan completed were used. The medium contained DMEM (with antibiotics) and 10% fetal calf serum. Incubation was at 37°C with 95% humidity.

[0084] Growth characteristics. Short-term growth experiments were performed using 24-well tissue culture plates (growth area 1.9 cm^2). About 10,000 cells were seeded into 6 sets of 24-well plates. The cells were allowed to attach and stabilize for 24hr in normal culture medium to achieve various final concentrations (range 40 to 500 μM). Culture medium was changed with the addition of test chemicals twice a week. The numbers of cells were counted after different days of treatment in 2 wells from each concentration of the test chemical using the normal method of cell trypsinization and counting using a Coulter counter. The third well in each category was fixed by cold methanol and stained with Giemsa stain for permanent record and for photography. Experiments were continued until the cultures became fully confluent and no further growth was possible.

[0085] Cell Attachment. These studies generally relate to cell migration potential and short term toxicity effects. The test compounds, as well as the controls, did not significantly affect the attachment frequency of human skin fibroblasts after 6 hours treatment at 40 to 200 μM; at 400 μM, attachment frequency for all test and control samples was reduced. No immediate toxicity was observed. In all further studies, the test or control compounds could be added to the culture medium at the time of cell seeding.

[0086] One Step Growth Curve. This short-term growth study (carried out over 11 days) tracks either stimulated or inhibited cell growth potential and provides information on delayed toxicity. Test compounds as well as controls were evaluated at 40, 80, 200, and 400 μM. The following results were obtained:

Compound	Increment in Cell Number (%)			
	40 μM	80 μM	200 μM	400 μM
6-(2-hydroxybenzylamino)-9-tetrahydropyranylpurine	+10	+10	toxic	toxic
6-(3-hydroxybenzylamino)-9-tetrahydropyranylpurine	+20	+25	0	-
6-(2-methoxybenzylamino)-9-tetrahydropyranylpurine	+30	+20	+10	> -50
6-(2, 5-dimethoxybenzylamino)-9-tetrahydropyranylpurine	+5	+10	> -50	> -50
Kinetin (control)	+5	+10	-30	-40
6-furfurylamino-9-tetrahydropyanylpuine (control)	+20	+20	< +5	> -50

[0087] Cell Morphology. Cells from the above cultures were examined for morphology at day 6 and day 11 to assess overall health of the cells. Cultures using the test compounds as well as a control (only 6-furfurylamino-9-tetrahydropyanylpuine was used) looked healthy and maintained their spindle shape in finger print-like arrays with low *intra* cellular debris and no cell enlargement for all dose rates.

[0088] Mitochondrial activity. Cell survival after exposure to various doses was measured with a 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay. About 5,000 cells were seeded per well in a 96-well plate 24 hours before the experiment. Cells were then treated with various doses of the individual test and control compounds. The wells were washed in Hank's and new medium was added. After three days, MTT (Sigma, M2128) was added at 0.5 mg/ml in medium. After 4 hours, MTT was removed and isopropanol and HCl were added to dissolve the MTT crystals for 12-16 hours. The absorbance was measured at 595 nm.

[0089] Test compounds 6-(2-hydroxybenzylamino)-9-tetrahydropyranylpurine, 6-(3-hydroxybenzylamino)-9-tetrahydropyranylpurine, and 6-(2-methoxybenzylamino)-9-tetrahydropyranylpurine and both controls resulted in stimulated cell viability by up to about 20% for does rates up to about 50 μM. Test compound 6-(2,5-dimethoxybenzylamino)-9-tetrahydropyranylpurine did not show any stimulation at similar dose rates. At does rates about about 100 μM, all test compounds and controls showed a decline in activity.

[0090] Lysosomal activity. Neutral red is preferentially taken up into the lysosomes of the cell. Fibroblast cells were maintained in culture and exposed to test compounds over a range of concentrations. The cultures were visually examined after 72 hours, and the number of viable cells and/or the total cell protein content determined by the neutral red uptake method. This assay only detects viable cells. Any compound having a localized effect upon the lysosomes will, therefore, result in an artificially low (or possibly high) reflection of cell viability and cell number. This factor does, however, make the system useful to detect those test compounds which selectively affect the lysosomes, especially when it is used in conjunction with other tests capable of determining cell number.

[0091] The neutral red assay was also used to evaluate and rank the cytotoxicity ot the test compounds. Individual wells of a 96-well tissue culture microtiter plate were inoculated with 0.2 ml of the appropriate media containing cells

(usually 3 x 10^3 cells). After 1 to 2 days of incubation, the media were removed and replaced with unamended (control) medium or with medium amended with varied concentrations of the compound to be tested. After 3 days of exposure to the test compound, the media was removed and replaced with media containing 0.001 % neutral red. The assay plate was then returned to the incubator for another 3 hours to allow for uptake of the supravital dye into the lysosomes of viable cells. Thereafter, the media was removed and the cells rapidly washed with 0.5% formaldehyde-1 % $CaCl_2$ followed by 0.2 ml of a solution of 1 % acetic acid-50% ethanol to extract the dye from the cells. After 10 min at room temperature and a brief but rapid agitation on a microtiter plate shaker, the plates were transferred to a micro plate spectrophotometer equipped with a 540-nm filter to measure the absorbance of the extracted dye.

[0092] The staining pattern for the neutral red assay showed cells undergoing autophagy (removal of cellular garbage) in all test compounds. Neutral red analysis showed a different toxicity profile from that obtained using mitochondrial activity. The following results were obtained:

	Relative Activity	Maximum Concentration (μM)
6-(2-hydroxybenzylamino)-9-tetrahydropyranylpurine	high	200
6-(3-hydroxybenzylamino)-9-tetrahydropyranylpurine	high	80
6-(2-methoxybenzylamino)-9-tetrahydropyranylpurine	high	200
6-(2,5-dimethoxybenzylamino)-9-tetrahydropyranylpurine	highest	40
Kinetin (control)	moderate	80
6-furfurylamino-9-tetrahydropyanylpuine (control)	high	80

[0093] Pre-treatment of the test compounds and controls at various doses improved the lysosomal turn-over rate over the untreated cells at various degrees as shown in the table below.

	Increased Activity (%)
6-(2-hydroxybenzylamino)-9-tetrahydropyranylpurine	10 - 30
6-(3-hydroxybenzylamino)-9-tetrahydropyranylpurine	15 - 20
6-(2-methoxybenzylamino)-9-tetrahydropyranylpurine	10 - 30
6-(2,5-dimethoxybenzylamino)-9-tetrahydropyranylpurine	20 - 45
Kinetin (control)	10 - 15
6-furfurylamino-9-tetrahydropyanylpuine (control)	30 - 40

Rejuvenation studies and cell survival.

[0094] The effect of the test compounds on morphology of nearing to senescent cells was used to determine if they could delay or maintain age-related alterations in tcell morphology. Late passage cells nearing to senescence were performed using 12-well tissue culture plates. About 10,000 cells were seeded into two sets of 12-well plates. The cells were allowed to attach and stabilize for 24 hrours in normal culture medium to achieve various final concentrations (range 40 to 200 μM). The numbers of cells were counted after 10 and 20 days of treatment in 2 wells from each concentration of the test compound using the normal cell trypsinization method with counting with Coulter counter. The third well in each category was fixed by cold methanol and stained with Giemsa stain for permanent record and for photography. The experiment was carried on for a period of twenty days.

[0095] None of the test compounds caused detrimental or lethal effects on the health of the cells even after 20 days of prolonged pre-treatment. After 10 days there were no significant differences in the appearance of cells. Overall, there was no significant cell enlargement and an absence of multinucleate cells with reduced levels of cellular debris. The test compounds at dose rates of 40 and 80 μM led to observable beneficial age effects after 20 days.

[0096] Survival quantifying by cell number. Equal numbers of senescent cells (at a density of 1.5 x 10^3) were seeded in separate flasks and were treated with different concentrations of test compounds. Cell numbers were determined by using a Coulter counter after trypsinization and resuspension of cells after 10 and 20 days of treatment.

[0097] Nearing to senescence cells had no significant increase in cell numbers due to treatment with test compounds or control compounds up to 80 μM. Overall, the cells looked better but did not increase in numbers. However, a significant reduction In cell numbers was observed at dose rates above 80 μM.

[0098] DNA duplication and detection. Toxicity studies are performed using the BrdU-assay (5-Bromo-2'-deoxy-uridine labelling and detection using Elisa plate reader). This assay is based on the measurement of incorporation of 5-bromo-2-deaoxyuridine during DNA synthesis as a marker for cell proliferation. Proportion of cells undergoing DNA duplication, and thus entering the next round of cell division, was determined by labeling the cells with bromodeoxyuridine, using a commercially available kit (Roche Diagnostics GmbH). The cells were cultured in a micro titre 96 well plate. BrdU was added to the culture medium and was Incorporated into freshly synthesized DNA (resulting concentration110 μM). The plate was then incubated for about 2-18 hours and fixed with 200 μl ethanol fixative (0.5 μM ethanol/HCL) after washing with PBS. Treatment with 100 μl of nuclease working solution (dilution 1:100 with incubation buffer) per well for 30 min at 37°C in absence of CO_2 improves the accessibility of the BrdU by the antibody detection. 100 μl of anti-BrdU -POD, Fab fragments are added with 9.9 μl of PBS and BSA (final concentration 200 μg/ml); the antibody conjugate was removed and washed with PBS. The final step involves addition of 100 μl of peroxidase per well incubated at room temperature until positive samples showed a green colour, which was clearly distinguishable from the color of pure peroxidase substrate. The absorbance was measured at 405 nm with reference at 490 nm and was directly correlated to the level of BrdU incorporated in the cell.

[0099] Two of test compounds (6-(2-hydroxybenzylamino)-9-tetrahydropyranylpurine and 6-(2-methoxybenzylamino)-9-tetrahydropyranylpurine) showed only a slight reduction (< 5%) in cell growth or division at the highest dosage rate of 200μM. The other test compounds as well as the two test compounds just mentioned at lower rates did not significantly effect cell growth or division. Thus, cell growth or division appeared normal.

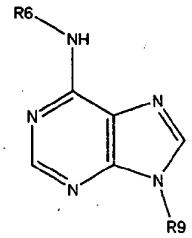
[0100] Cytoskeletal organization. One of the crucial age-related changes during cellular ageing *in vitro* is the alterations in the cytoskeletal organization. Typically young fibroblasts have diffused pattern of actin homogenously dispersed through out the cell with little or no polymerization as compared highly polymerized rod like staining pattern observed most commonly in enlarged and senescent cells. The pattern of cytoskeletal actin staining was studied by staining the cells with fluorescent ligand FITC-labelled Phalloidin, using a fluorescence microscope. The treated and untreated cells were then visually examined to identify any changes within the cells. No controls were used.

[0101] The no visible alterations in the cytoskeletal organization of cells treated with test compounds were observed. There was no apparent change or shift from diffused pattern of actin homogenously dispersed through out the cell (young phenotype) to rod like polymerized actin filaments (aged phenotype).

[0102] Based on these short-term evaluations (i.e., cell attachment, survival, growth, mitochondrial activity, lysosomal activity, reversion studies, and morphology of early passage and nearing to senescence cultures of adult human skin fibroblasts) it appears that all four test compounds would be suitable for use in cosmetic or other formulations for treatment of skin, including human skin, with 6-(2-hydroxybenzylamino)-9-tetrahydropyranylpurine, 6-(3-hydroxybenzylamino)-9-tetrahydropyranylpurine, and 6-(2-methoxybenzylamino)-9-tetrahydropyranyipurine being more preferred.

Claims

1. 6,9-Disubstituted purine derivatives of the general formula I



I

and their pharmaceutically acceptable salts,
wherein R6 is an alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycle, heterocycloalkyl, heteroalkyl, or arylalkyl group containing at least one hydroxyl substitution thereon, and
wherein R9 is a tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, or 1-ethoxyethyl group;
wherein alkyl denotes a branched or unbranched alkyl chain containing 1 to 8 carbon atoms, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of hydroxyl, halogen, alkyloxy, aryloxy, alkylamino, arylamino, amino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, alkyloxycarbonylamino, aryloxycarbonylamino, aryl, heterocycle, and heter-

oaryl;
wherein alkenyl denotes a branched or unbranched alkenyl chain containing 2 to 7 carbon atoms with at least one double bond therein, which is optionally substituted independently with 1 to 6 substituents selected from the group containing halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group,
wherein alkynyl denotes a branched or unbranched alkynyl chain containing 2 to 7 carbon atoms with at least one tripple bond therein, which is optionally substituted independently with 1 to 6 substituents selected from the group consisting of halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, alkyloxycarbonylamino, and aryloxycarbonylamino group;
wherein cycloalkyl denotes a monocyclic or polycyclic alkyl group containing 3 to 15 carbon atoms, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein aryl denotes a aromatic carbocyclic group containing 6 to 18 carbon atoms with at least one aromatic ring or a multiple condensed ring with at least one aromatic ring, which is substituted independently with 1 to 7 substituents selected from the group consisting of halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group;
wherein heterocycle denotes a heterocyclic group containing 4 to 9 carbon atoms and at least one heteroatom selected from the group consisting of oxygen atom, sulphur atom, and nitrogen atom, which is optionally substituted independently at with 1 to 7 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heteroaryl denotes a heterocycle in which at least one heterocyclic ring is aromatic, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heterocycloalkyl denotes a -R_a-Het group where Het is a heterocycle group and R_a is an alkyl group, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heteroarylalkyl denotes a -R_a-HetAr group where HetAr is an heteroaryl group and R_a is as defined above;
wherein arylalkyl denotes a -R_b-Ar group where Ar is aryl group and R_b is a branched or unbranched alkyl chain containing 1 to 6 carbon atoms, which is optionally substituted independently with 1 to 5 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group;
wherein halogen denotes a fluorine, bromine, chlorine, or iodine atom,
wherein hydroxy denotes an -OH group,
wherein mercapto denotes a -SH group,
wherein amino denotes a -NH_2 group,
wherein carbamoyl denotes a -$CONH_2$ group.
wherein cyano denotes a -CN group,
wherein carboxyl denotes a -COOH group,
wherein nitro denotes a -NO_2 group,
wherein sulpho denotes a -SO_3R_c group where R_c is hydrogen or alkyl,
wherein sulphamido denotes the $SO_2NR_cR_c$' group where R_c and R_c' are independently hydrogen or alkyl,
wherein acyl denotes a -$C(O)R_d$ group, wherein R_d is alkyl, aryl, arylalkyl or cycloalkyl,
wherein acyloxy denotes a -$O\text{-}C(O)R_e$ group where R_e is alkyl, aryl, or heterocycle,
wherein acylamino denotes a -$NHCOR_f$ group, wherein R_f is alkyl, heterocycle, or aryl,
wherein alkyloxycarbonylamino denotes a -$NHCOOR_g$ group where R_g is alkyl or cycloalkyl,
wherein aryloxycarbonylamino denotes a -$NHCOOR_h$ group where R_h is aryl,
wherein alkyloxy denotes a -OR_h group where R_h is alkyl, cycloalkyl, or arylalkyl,
wherein aryloxy denotes a -OR_g group where R_g is aryl,
wherein alkylamino denotes a -NR_iR_j group where R_i is hydrogen, alkyl, or heterocycle and R_j is alkyl or heterocycle,

wherein arylamino denotes a -NR_kR_h group where R_k is hydrogen or aryl and R_h is alkyl, aryl, or heterocycle,
wherein alkylthio denotes a -SR_h group where R_h is as defined above, and
wherein arylthio denotes a -SR_g group where R_g is as defined above.

2. The 6,9-disubstituted purine derivatives according to claim 1 selected from the group consisting of 6-(2-hydroxycyclopropylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxycyclobutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxycyclohexylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-5-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,3-dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,4-dihydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,5-dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dihydroxy-4-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-5-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine; 6-(4-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dimethyl-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dibromo-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxymethyl-3-methylallyl)amino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(Z)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(1'-ethyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-4-morfolinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-1-pyrolidinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-6-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-carboxy-4-hydroxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methoxylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine and their pharmaceutically acceptable salts.

3. The 6,9-disubstituted purine derivatives according to claim 2 selected from the group consisting of 6-(4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-

methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl) purine, 6-(E)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(1'-methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, and their pharmaceutically acceptable salts.

4. A cosmetic composition comprising an effective amount of one or more 6,9-disubstituted purine derivatives or their pharmaceutically acceptable salts and one or more excipients, wherein the 6,9-disubstituted purine derivatives are as defined in claim 1.

5. The cosmetic composition of claim 4, wherein the 6,9-disubstituted purine derivatives are as defined in claim 2.

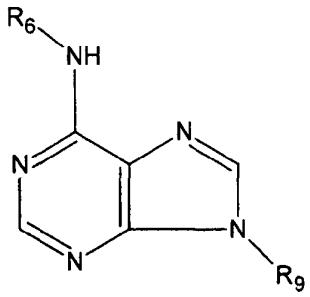
6. The cosmetic composition of claim 4, wherein the 6,9-disubstituted purine derivatives are as defined in claim 3.

7. 6,9-disubstituted purine derivatives according to claim 1 for use in inhibiting ageing or senescence of mammalian epidermal cells.

8. 6,9-disubstituted purine derivatives according to claim 2 for use in inhibiting ageing or senescence of mammalian epidermal cells.

9. 6,9-disubstituted purine derivatives according to claim 3 for use in inhibiting ageing or senescence of mammalian epidermal cells.

10. 6,9-disubstituted purine derivatives of the general formula I, or their pharmaceutically acceptable salts,



I

wherein R6 is an alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycle, heterocycloalkyl, heteroalkyl, or arylalkyl group containing at least one hydroxyl substitution thereon, and
wherein R9 is a tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, or 1-ethoxyethyl group;
wherein alkyl denotes a branched or unbranched alkyl chain containing 1 to 8 carbon atoms, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of hydroxyl, halogen, alkyloxy, aryloxy, alkylamino, arylamino, amino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, alkyloxycarbonylamino, aryloxycarbonylamino, aryl, heterocycle, and heteroaryl;
wherein alkenyl denotes a branched or unbranched alkenyl chain containing 2 to 7 carbon atoms with at least one double bond therein, which is optionally substituted independently with 1 to 6 substituents selected from the group containing halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group,
wherein alkynyl denotes a branched or unbranched alkynyl chain containing 2 to 7 carbon atoms with at least one tripple bond therein, which is optionally substituted independently with 1 to 6 substituents selected from the group consisting of halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, alkyloxycarbonylamino, and

aryloxycarbonylamino group;
wherein cycloalkyl denotes a monocyclic or polycyclic alkyl group containing 3 to 15 carbon atoms, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein aryl denotes a aromatic carbocyclic group containing 6 to 18 carbon atoms with at least one aromatic ring or a multiple condensed ring with at least one aromatic ring, which is substituted independently with 1 to 7 substituents selected from the group consisting of halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group;
wherein heterocycle denotes a heterocyclic group containing 4 to 9 carbon atoms and at least one heteroatom selected from the group consisting of oxygen atom, sulphur atom, and nitrogen atom, which is optionally substituted independently at with 1 to 7 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heteroaryl denotes a heterocycle in which at least one heterocyclic ring is aromatic, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heterocycloalkyl denotes a -R_a-Het group where Het is a heterocycle group and R_a is an alkyl group, which is optionally substituted independently with 1 to 7 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino, and alkyloxycarbonylamino group;
wherein heteroarylalkyl denotes a -R_a-HetAr group where HetAr is an heteroaryl group and R_a is as defined above;
wherein arylalkyl denotes a -R_b-Ar group where Ar is aryl group and R_b is a branched or unbranched alkyl chain containing 1 to 6 carbon atoms, which is optionally substituted independently with 1 to 5 substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyl, cyano, nitro, carbamoyl, sulpho, sulphamido, acyl, acylamino, acyloxy, alkylthio, arylthio, cycloalkyl, aryloxycarbonylamino and alkyloxycarbonylamino group;
wherein halogen denotes a fluorine, bromine, chlorine, or iodine atom,
wherein hydroxy denotes an -OH group,
wherein mercapto denotes a -SH group,
wherein amino denotes a -NH_2 group,
wherein carbamoyl denotes a -$CONH_2$ group.
wherein cyano denotes a -CN group,
wherein carboxyl denotes a -COOH group,
wherein nitro denotes a -NO_2 group,
wherein sulpho denotes a -SO_3R_c group where R_c is hydrogen or alkyl,
wherein sulphamido denotes the $SO_2NR_cR_c$' group where R_c and R_c' are independently hydrogen or alkyl,
wherein acyl denotes a -$C(O)R_d$ group, wherein R_d is alkyl, aryl, arylalkyl or cycloalkyl,
wherein acyloxy denotes a -O-$C(O)R_e$ group where R_e is alkyl, aryl, or heterocycle,
wherein acylamino denotes a -$NHCOR_f$ group, wherein R_f is alkyl, heterocycle, or aryl,
wherein alkyloxycarbonylamino denotes a -$NHCOOR_g$ group where R_g is alkyl or cycloalkyl,
wherein aryloxycarbonylamino denotes a -$NHCOOR_h$ group where R_h is aryl,
wherein alkyloxy denotes a -OR_h group where R_h is alkyl, cycloalkyl, or arylalkyl,
wherein aryloxy denotes a -OR_g group where R_g is aryl,
wherein alkylamino denotes a -NR_iR_j group where R_i is hydrogen, alkyl, or heterocycle and R_j is alkyl or heterocycle,
wherein arylamino denotes a -NR_kR_h group where R_k is hydrogen or aryl and R_h is alkyl, aryl, or heterocycle,
wherein alkylthio denotes a -SR_h group where R_h is as defined above, and
wherein arylthio denotes a -SR_g group where R_g is as defined above, for use in the treatment of skin disease states in a mammal.

11. 6,9-disubstituted purine derivatives according to claim 10 selected from the group consisting of 6-(2-hydroxycyclopropylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxycyclobutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxycyclohexylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hy-

droxy-3-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-5-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl) purine, 6-(3-hydroxy-4-iodobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-bromobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-fluorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,3-dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,4-dihydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2,5-dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dihydroxy-4-chlorobenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-5-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3,5-dimethyl-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl) purine, 6-(3,5-dibromo-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxymethyl-3-methylallyl)amino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(Z)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(Z)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl) purine, 6-(1'-methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-3-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-4-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(2-hydroxy-4-morfolinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-hydroxy-1-pyrolidinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-6-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(3-carboxy-4-hydroxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-2-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine and their pharmaceutically acceptable salts
for use in the treatment of skin disease states in a mammal.

12. 6,9-disubstituted purine derivatives according to claim 10 selected from the group consisting of 6-(4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(E)-(1'-methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(1'-methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine, 6-(4-hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorobutyl, 1-ethoxyethyl)purine and their pharmaceutically acceptable salts for use in the treatment

of skin disease states in a mammal.

13. 6,9-disubstituted purine derivatives according to claim 1 or their pharmaceutically acceptable salts for use in the treatment of immunological responses resulting from, or associated with, inflammation on mammalian skin.

14. 6,9-disubstituted purine derivatives according to claim 2 or their pharmaceutically acceptable salts for use in the treatment of immunological responses resulting from, or associated with, inflammation on mammalian skin.

15. 6,9-disubstituted purine derivatives according to claim 3 or their pharmaceutically acceptable salts for use in the treatment of immunological responses resulting from, or associated with, inflammation on mammalian skin.

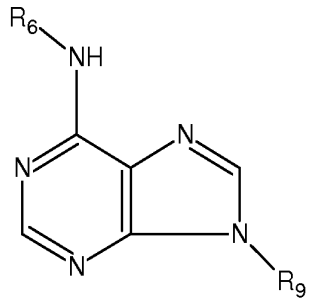
16. 6,9-disubstituted purine derivatives according to claim 1 or their pharmaceutically acceptable salts for use in ameliorating adverse effects of aging in mammalian cells.

17. 6,9-disubstituted purine derivatives according to claim 2 or their pharmaceutically acceptable salts for use in ameliorating adverse effects of aging in mammalian cells.

18. 6,9-disubstituted purine derivatives according to claim 3 or their pharmaceutically acceptable salts for use in ameliorating adverse effects of aging in mammalian cells.

Patentansprüche

1. 6,9-disubstituierte Purin-Derivate der allgemeinen Formel I



I

und deren pharmazeutisch akzeptable Salze,
worin R_6 Alkyl, Alkenyl, Alkynyl, Cycloalkyl, Aryl, Heterocyclyl, Heterocycloalkyl, Heteroalkyl oder Arylalkyl umfassend mindestens einen Hydroxylsubstituent bedeutet und
worin R_9 Tetrahydropyran-2-yl, Tetrahydrofuran-2-yl, 4-Chlorbutyl oder 1-Ethoxyethyl bedeutet;
worin Alkyl eine verzweigte oder nicht verzweigte Alkylkette umfassend 1 bis 8 Kohlenstoffatome bedeutet, die unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Hydroxyl, Halogen, Alkyloxy, Aryloxy, Alkylamino, Arylamino, Amino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Alkyloxykarbonylamino, Aryloxykarbonylamino, Aryl, Heterocyclus und Heteroaryl;
worin Alkenyl eine verzweigte oder nicht verzweigte Alkenylkette umfassend 2 bis 7 Kohlenstoffatome mit mindestens einer Doppelbindung bedeutet, die unabhängig durch 1 bis 6 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe umfassend die Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino,
worin Alkynyl eine verzweigte oder nicht verzweigte Alkynylkette umfassend 2 bis 7 Kohlenstoffatome mit mindestens einer Dreifachbindung bedeutet, die unabhängig durch 1 bis 6 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Alkyloxykarbonylamino und Aryloxykarbonylamino,
worin Cycloalkyl eine monocyclische oder polycyclische Alkylgruppe umfassend 3 bis 15 Kohlenstoffatome bedeutet, die unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus

den Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino,

worin Aryl eine aromatische karbocyclische Gruppe umfassend 6 bis 18 Kohlenstoffatome mit mindestens einem aromatischen Ring oder mit kondensierten Ringen mit mindestens einem aromatischen Ring bedeutet, das unabhängig durch 1 bis 7 Substituenten substituiert ist, ausgewählt aus einer Gruppe bestehend aus den Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino,

worin Heterocyclus eine heterocyclische Gruppe umfassend 4 bis 9 Kohlenstoffatome und mindestens einen Heteroatom ausgewählt aus einer Gruppe umfassend einen Sauerstoff-, Schwefel- und Stickstoffatom bedeutet, das unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino,

worin Heteroaryl einen Heterocyclus bedeutet, in dem mindestens ein heterocyclischer Ring aromatisch ist, und das unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Heterocycloalkyl eine -R_a-Het-Gruppe bedeutet, in der Het für einen Heterocyclus und R_a für eine Alkylgruppe stehen und das unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Heteroarylalkyl eine -R_a-HetAr-Gruppe bedeutet, in der HetAr eine Heteroarylgruppe ist und R_a oben definiert ist;

worin Arylalkyl eine -R_b-Ar-Gruppe bedeutet, in der Ar für eine Arylgruppe und R_b für eine verzweigte oder nicht verzweigte Kohlenstoffkette umfassend 1 bis 6 Kohlenstoffatome stehen und das unabhängig durch 1 bis 5 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Halogen einen Fluor-, Chlor-, Brom- oder Jodatom bedeutet,

worin Hydroxy eine -OH-Gruppe bedeutet,

worin Merkapto eine -SH-Gruppe bedeutet,

worin Amino eine -NH_2-Gruppe bedeutet,

worin Karbamoyl eine -$CONH_2$-Gruppe bedeutet,

worin Kyano eine -CN-Gruppe bedeutet,

worin Karboxyl eine -COOH-Gruppe bedeutet,

worin Nitro eine -NO_2-Grupp bedeutet,

worin Sulfo eine -SO_3R_c-Gruppe bedeutet, in der R_c für Wasserstoff oder Alkyl steht,

worin Sulfamido eine $SO_2NR_cR_c$'-Gruppe bedeutet, in der R_c und R_c' unabhängig voneinander für Wasserstoff oder Alkyl stehen,

worin Acyl eine -$C(O)R_d$-Gruppe bedeutet, in der R_d für Alkyl, Aryl, Arylalkyl oder Cycloalkyl steht,

worin Acyloxy eine -O-$C(O)R_e$-Gruppe bedeutet, in der R_e für Alkyl, Aryl oder Heterocyclus steht,

worin Acylamino eine -$NHCOR_f$-Gruppe bedeutet, in der R_f für Alkyl, Heterocyclus oder Aryl steht,

worin Alkyloxykarbonylamino eine -$NHCOOR_g$-Gruppe bedeutet, in der R_g für Alkyl oder Cycloalkyl steht,

worin Aryloxykarbonylamino eine -$NHCOOR_h$-Gruppe bedeutet, in der R_h für Aryl steht,

worin Alkyloxy eine -OR_h-Gruppe bedeutet, in der R_h für Alkyl, Cycloalkyl oder Arylalkyl steht,

worin Aryloxy eine -OR_g-Gruppe bedeutet, in der R_g für Aryl steht,

worin Alkylamino eine -NR_iR_j-Gruppe bedeutet, in der R_i für Wasserstoff, Alkyl oder Heterocyclus und R_j für Alkyl oder Heterocyclus stehen,

worin Arylamino eine -NR_kR_h-Gruppe bedeutet, in der R_k für Wasserstoff oder Aryl und R_h für Alkyl, Aryl oder Heterocyclus stehen,

worin Alkylthio eine -SR_h-Gruppe bedeutet, in der R_h oben definiert ist, und worin Arylthio eine -SR_g-Gruppe bedeutet, in der R_g oben definiert ist.

2. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 1, ausgewählt aus der Gruppe bestehend aus 6-(2-Hydroxycyclopropylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxycyclobutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxycyclohexylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-jodbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-5-jodbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-jodbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-brombenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-brombenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-brombenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-fluorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-fluorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-fluorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2,3-Dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2,4-Dihydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2,5-Dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3,5-Dihydroxy-4-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-5-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-2-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3,5-Dimethyl-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3,5-Dibrom-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxymethyl-3-methylallyl)amino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(Z)-(4-Hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(4-Hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(Z)-(1'-Methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(1'-Methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(1'-Methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-4-morpholinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-1-pyrolidinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-2-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-6-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Karboxy-4-hydroxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-2-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin und deren pharmazeutisch akzeptablen Salzen.

3. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 2, ausgewählt aus einer Gruppe bestehend aus 6-(4-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(4-Hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(1 '-Methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(1'-Methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl,

4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin und deren pharmazeutisch akzeptablen Salzen.

4. Kosmetische Komposition umfassend eine wirksame Menge eines oder mehrerer 6,9-disubstituierter Purin-Derivaten oder deren pharmazeutisch akzeptabler Salze und einen oder mehrere Exzipienten, wobei die 6,9-disubstituierte Purin-Derivate im Anspruch 1 definiert sind.

5. Kosmetische Komposition nach dem Anspruch 4, worin die 6,9-disubstituierten Purin-Derivate im Anspruch 2 definiert sind.

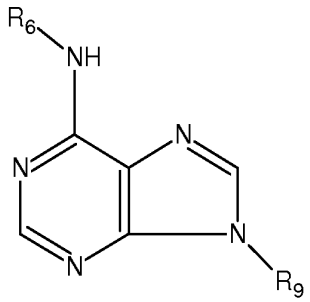
6. Kosmetische Komposition nach dem Anspruch 4, worin die 6,9-disubstituierten Purin-Derivate im Anspruch 3 definiert sind.

7. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 1 zur Anwendung in der Alterungsinhibition oder Seneszenz der Säugerepidermalzellen.

8. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 2 zur Anwendung in der Alterungsinhibition oder Seneszenz der Säugerepidermalzellen.

9. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 3 zur Anwendung in der Alterungsinhibition oder Seneszenz der Säugerepidermalzellen.

10. 6,9-disubstituierte Purin-Derivate der allgemeinen Formel I oder deren pharmazeutisch akzeptable Salze,



I

worin R_6 Alkyl, Alkenyl, Alkynyl, Cycloalkyl, Aryl, Heterocyclus, Heterocycloalkyl, Heteroalkyl oder Arylalkyl umfassend mindestens einen Hydroxylsubstituent bedeutet und
worin R_9 Tetrahydropyran-2-yl, Tetrahydrofuran-2-yl, 4-Chlorbutyl oder 1-Ethoxyethyl bedeutet;
worin Alkyl eine verzweigte oder nicht verzweigte Alkylkette umfassend 1 bis 8 Kohlenstoffatome bedeutet, die unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Hydroxyl, Halogen, Alkyloxy, Aryloxy, Alkylamino, Arylamino, Amino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Alkyloxykarbonylamino, Aryloxykarbonylamino, Aryl, Heterocyclus und Heteroaryl;
worin Alkenyl eine verzweigte oder nicht verzweigte Alkenylkette umfassend 2 bis 7 Kohlenstoffatome mit mindestens einer Doppelbindung bedeutet, die unabhängig durch 1 bis 6 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe umfassend die Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;
worin Alkynyl eine verzweigte oder nicht verzweigte Alkynylkette umfassend 2 bis 7 Kohlenstoffatome mit mindestens einer Dreifachbindung bedeutet, die unabhängig durch 1 bis 6 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Alkyloxykarbonylamino und Aryloxykarbonylamino;
worin Cycloalkyl eine monocyclische oder polycyclische Alkylgruppe umfassend 3 bis 15 Kohlenstoffatome bedeutet, die unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus

den Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Aryl eine aromatische karbocyclische Gruppe umfassend 6 bis 18 Kohlenstoffatome mit mindestens einem aromatischen Ring oder mit kondensierten Ringen mit mindestens einem aromatischen Ring bedeutet, das unabhängig durch 1 bis 7 Substituenten substituiert ist, ausgewählt aus einer Gruppe bestehend aus den Gruppen Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Heterocyclus eine heterocyclische Gruppe umfassend 4 bis 9 Kohlenstoffatome und mindestens einen Heteroatom ausgewählt aus einer Gruppe umfassend einen Sauerstoff-, Schwefel- und Stickstoffatom bedeutet, und der unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Heteroaryl einen Heterocyclus bedeutet, in dem mindestens ein heterocyclischer Ring aromatisch ist, und das unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Heterocycloalkyl eine -R_a-Het-Gruppe bedeutet, in der Het für einen Heterocyclus und R_a für eine Alkylgruppe stehen und die unabhängig durch 1 bis 7 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Heteroarylalkyl eine -R_a-HetAr-Gruppe bedeutet, in der HetAr eine Heteroarylgruppe ist und R_a oben definiert ist;

worin Arylalkyl eine -R_b-Ar-Gruppe bedeutet, in der Ar für eine Arylgruppe und R_b für eine verzweigte oder nicht verzweigte Kohlenstoffkette umfassend 1 bis 6 Kohlenstoffatome stehen und die unabhängig durch 1 bis 5 Substituenten substituiert werden kann, ausgewählt aus einer Gruppe bestehend aus den Gruppen Alkyl, Halogen, Hydroxyl, Alkyloxy, Aryloxy, Amino, Alkylamino, Arylamino, Merkapto, Karboxyl, Kyano, Nitro, Karbamoyl, Sulfo, Sulfamido, Acyl, Acylamino, Acyloxy, Alkylthio, Arylthio, Cycloalkyl, Aryloxykarbonylamino und Alkyloxykarbonylamino;

worin Halogen einen Fluor-, Chlor-, Brom- oder Jodatom bedeutet,

worin Hydroxy eine -OH-Gruppe bedeutet,

worin Merkapto eine -SH-Gruppe bedeutet,

worin Amino eine -NH_2-Gruppe bedeutet,

worin Karbamoyl eine -$CONH_2$-Gruppe bedeutet,

worin Kyano eine -CN-Gruppe bedeutet,

worin Karboxyl eine -COOH-Gruppe bedeutet,

worin Nitro eine -NO_2-Gruppe bedeutet,

worin Sulfo eine -SO_3R_c-Gruppe bedeutet, in der R_c für Wasserstoff oder Alkyl steht,

worin Sulfamido eine $SO_2NR_cR_c$'-Gruppe bedeutet, in der R_c und R_c' unabhängig voneinander für Wasserstoff oder Alkyl stehen,

worin Acyl eine -$C(O)R_d$-Gruppe bedeutet, in der R_d für Alkyl, Aryl, Arylalkyl oder Cycloalkyl steht,

worin Acyloxy eine -O-$C(O)R_e$-Gruppe bedeutet, in der R_e für Alkyl, Aryl oder Heterocyclus steht,

worin Acylamino eine -$NHCOR_f$-Gruppe bedeutet, in der R_f für Alkyl, Heterocyclus oder Aryl steht,

worin Alkyloxykarbonylamino eine -NHCOORg-Gruppe bedeutet, in der R_g für Alkyl oder Cycloalkyl steht,

worin Aryloxykarbonylamino eine -$NHCOOR_h$-Gruppe bedeutet, in der R_h für Aryl steht,

worin Alkyloxy eine -OR_h-Gruppe bedeutet, in der R_h für Alkyl, Cycloalkyl oder Arylalkyl steht,

worin Aryloxy eine -OR_g-Gruppe bedeutet, in der R_g für Aryl steht,

worin Alkylamino eine -NR_iR_j-Gruppe bedeutet, in der R_i für Wasserstoff, Alkyl oder Heterocyclus und R_j für Alkyl oder Heterocyklus stehen,

worin Arylamino eine -NR_kR_h-Gruppe bedeutet, in der R_k für Wasserstoff oder Aryl und R_h für Alkyl, Aryl oder Heterocyclus stehen,

worin Alkylthio eine -SR_h-Gruppe bedeutet, in der R_h oben definiert ist, und worin Arylthio eine -SR_g-Gruppe bedeutet, in der R_g oben definiert ist.

zur Anwendung bei der Behandlung von Hauterkrankungen bei den Säugern.

11. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 10, ausgewählt aus einer Gruppe bestehend aus 6-(2-Hydroxycyclopropylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxycyclobutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxycyclohexylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-jodbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-5-jodbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-jodbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-brombenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-brombenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-brombenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-fluorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-fluorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-fluorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2,3-Dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2,4-dihydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2,5-Dihydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3,5-Dihydroxy-4-chlorbenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-5-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-4-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-2-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3,5-Dimethyl-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3,5-Dibrom-4-hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxymethyl-3-methylallyl)amino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(Z)-(4-Hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(4-Hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(Z)-(1'-Methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(1'-Methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(1'-Methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-3-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-4-pyridylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(2-Hydroxy-4-morfolinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Hydroxy-1-pyrolidinylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-2-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-6-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(3-Karboxy-4-hydroxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-2-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin und deren pharmazeutisch akzeptablen Salzen
zur Anwendung bei der Behandlung von Hauterkrankungen bei den Säugern.

12. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 10, ausgewählt aus einer Gruppe bestehend aus 6-(4-Hydroxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxybenzylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(4-Hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(E)-(1 '-Methyl-4-hydroxy-3-methylbut-2-en-1-ylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbu-

tyl, 1-ethoxyethyl)purin, 6-(1'-Methyl-4-hydroxy-3-methylbutylamino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methylanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin, 6-(4-Hydroxy-3-methoxyanilino)-9-(tetrahydropyran-2-yl, tetrahydrofuran-2-yl, 4-chlorbutyl, 1-ethoxyethyl)purin und deren pharmazeutisch akzeptablen Salzen zur Anwendung bei der Behandlung von Hauterkrankungen bei den Säugern.

13. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 1 oder deren pharmazeutisch akzeptable Salze zur Anwendung bei der Behandlung immunologischer Reaktionen als Folgen oder betreffend Hautentzündungen bei den Säugern.

14. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 2 oder deren pharmazeutisch akzeptable Salze zur Anwendung bei der Behandlung immunologischer Reaktionen als Folgen oder betreffend Hautentzündungen bei den Säugern.

15. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 3 oder deren pharmazeutisch akzeptable Salze zur Anwendung bei der Behandlung immunologischer Reaktionen als Folgen oder betreffend Hautentzündungen bei den Säugern.

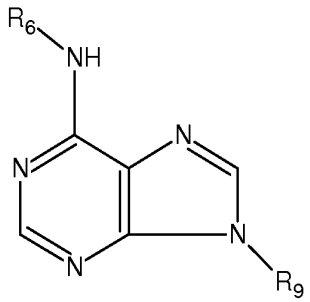
16. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 1 oder deren pharmazeutisch akzeptable Salze zur Anwendung bei der Verbesserung unerwünschter Alterungsauswirkungen auf die Säugerzellen.

17. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 2 oder deren pharmazeutisch akzeptable Salze zur Anwendung bei der Verbesserung unerwünschter Alterungsauswirkungen auf die Säugerzellen.

18. 6,9-disubstituierte Purin-Derivate nach dem Anspruch 3 oder deren pharmazeutisch akzeptable Salze zur Anwendung bei der Verbesserung unerwünschter Alterungsauswirkungen auf die Säugerzellen.

Revendications

1. Dérivés de purine 6,9-disubstituée selon la formule générale I



I

et leurs sels pharmaceutiquement acceptables,
dans laquelle R_6 est un groupe alkyle, alcényle, alcynyle, cycloalkyle, aryle, hétérocycle, hétérocycloalkyle, hétéroalkyle ou arylalkyle comprenant au moins un substituant hydroxyle et
dans laquelle R_9 est un groupe tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle ou 1-éthoxyéthyle;
dans laquelle l'alkyle représente une chaîne alkyle ramifiée ou non ramifiée contenant 1 à 8 atomes de carbone pouvant, le cas échéant, être substituée indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes hydroxyle, halogène, alkyloxy, aryloxy, alkylamino, arylamino, amino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, alkyloxycarbonylamino, aryloxycarbonylamino, aryle, hétérocycle et hétéroaryle;
dans laquelle l'alcényle représente une chaîne alcényle ramifiée ou non ramifiée contenant 2 à 7 atomes de carbone avec au moins une liaison double, pouvant, le cas échéant, être substituée indépendamment par 1 à 6 substituants choisis parmi un groupe contenant de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cy-

cloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino,
dans laquelle l'alcynyle représente une chaîne alcynyle ramifiée ou non ramifiée contenant 2 à 7 atomes de carbone avec au moins une liaison triple, pouvant, le cas échéant, être substituée indépendamment par 1 à 6 substituants choisis parmi un groupe constitué de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, alkyloxycarbonylamino et aryloxycarbonylamino,
dans laquelle le cycloalkyle représente un groupe alkyle monocyclique ou polycyclique contenant 3 à 15 atomes de carbone pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino,
dans laquelle l'aryle représente un groupe aromatique carbocyclique contenant 6 à 18 atomes de carbone avec au moins un cycle aromatique ou avec un cycle multiple condensé avec au moins un cycle aromatique lequel est substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino,
dans laquelle l'hétérocycle représente un groupe hétérocyclique contenant 4 à 9 atomes de carbone avec au moins un hétéroatome choisi parmi un groupe comprenant l'atome d'oxygène, de soufre et d'azote et pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino,
dans laquelle l'hétéroaryle représente un hétérocycle dans lequel au moins un cycle hétérocyclique est aromatique et pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino ;
dans laquelle l'hétérocycloalkyle représente un groupe -R_a-Het dans lequel Het est un groupe hétérocycle et R_a est un groupe alkyle pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino
dans laquelle l'hétéroarylalkyle représente un groupe -R_a-HetAr, dans lequel HetAr est un groupe hétéroaryle et R_a est défini ci-dessus ;
dans laquelle l'arylalkyle représente un groupe -R_b-Ar, dans lequel Ar est un groupe aryle et R_b est une chaîne de carbone ramifiée ou non ramifiée contenant 1 à 6 atomes de carbone et pouvant, le cas échéant, être substituée indépendamment par 1 à 5 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino ;
dans laquelle l'halogène représente un atome de fluor, brome, chlore ou iode, dans laquelle hydroxy représente un groupe -OH,
dans laquelle mercapto représente un groupe -SH,
dans laquelle amino représente un groupe -NH_2,
dans laquelle carbamoyl représente un groupe -$CONH_2$,
dans laquelle cyano représente un groupe -CN,
dans laquelle carboxyle représente un groupe -COOH,
dans laquelle nitro représente un groupe -NO_2,
dans laquelle sulfo représente un groupe -SO_3R_c, dans lequel R_c est hydrogène ou alkyle,
dans laquelle sulfamido représente un groupe $SO_2NR_cR_c$', dans lequel R_c et R_c' sont indépendamment hydrogène ou alkyle,
dans laquelle acyle représente un groupe -$C(O)R_d$, dans lequel R_d est alkyle, aryle, arylalkyle ou cycloalkyle,
dans laquelle acyloxy représente un groupe -O-$C(O)R_e$, dans lequel R_e est alkyle, aryle ou hétérocycle,
dans laquelle acylamino représente un groupe -$NHCOR_f$, dans lequel R_f est alkyle, hétérocycle ou aryle,
dans laquelle alkyloxycarbonylamino représente un groupe -$NHCOOR_g$, dans lequel R_g est alkyle ou cycloalkyle,
dans laquelle aryloxycarbonylamino représente un groupe -$NHCOOR_h$, dans lequel R_h est aryle,
dans laquelle alkyloxy représente un groupe -OR_h, dans lequel R_h est alkyle, cycloalkyle ou arylalkyle,
dans laquelle aryloxy représente un groupe -OR_g, dans lequel R_g est aryle, dans laquelle alkylamino représente un groupe -NR_iR_j, dans lequel R_i est hydrogène, alkyle ou hétérocycle et R_j est alkyle ou hétérocycle,

dans laquelle arylamino représente un groupe -NR_kR_h, dans lequel R_k est hydrogène ou aryle et R_h est alkyle, aryle ou hétérocycle,
dans laquelle alkylthio représente un groupe -SR_h, dans lequel R_h est défini ci-dessus, et
dans laquelle arylthio représente un groupe -SR_g, dans lequel R_g est défini ci-dessus.

2. Dérivés de purine 6,9-disubstituée selon la revendication 1, choisis parmi le groupe constitué de 6-(2-hydroxycyclopropylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxycyclobutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxycyclohexylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-chlorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-chlorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-chlorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-iodobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-5-iodobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-iodobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-bromobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-bromobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-bromobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-fluorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-fluorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-fluorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2,3-dihydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2,4-dihydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2,5-dihydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3,5-dihydroxy-4-chlorbenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-5-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-2-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3,5-diméthyl-4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3,5-dibromo-4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxyméthyl-3-méthylallyl)amino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(Z)-(4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(Z)-(1'-méthyl-4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(1'-méthyl-4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(1'-méthyl-4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-pyridylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-pyridylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-4-morpholinylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-1-pyrolidinylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-2-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-6-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-carboxy-4-hydroxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-2-méthoxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine et de leurs sels pharmaceutiquement acceptables.

3. Dérivés de purine 6,9-disubstituée selon la revendication 2, choisis parmi le groupe constitué de 6-(4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(1'-méthyl-4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(1'-méthyl-4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine et de leurs sels pharmaceutiquement acceptables.

4. Composition cosmétique comprenant une quantité efficace d'un ou de plusieurs dérivés de purine 6,9-disubstituée ou de leurs sels pharmaceutiquement acceptables et un ou plusieurs excipients, dans laquelle les dérivés de purine 6,9-disubstituée sont tels que définis dans la revendication 1.

5. Composition cosmétique selon la revendication 4, dans laquelle les dérivés de purine 6,9-disubstituée sont tels que définis dans la revendication 2.

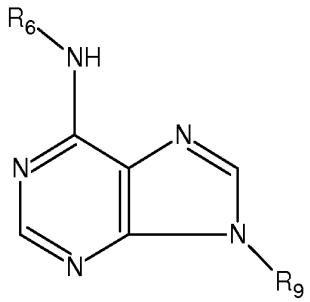
6. Composition cosmétique selon la revendication 4, dans laquelle les dérivés de purine 6,9-disubstituée sont tels que définis dans la revendication 3.

7. Dérivés de purine 6,9-disubstituée selon la revendication 1 pour utilisation dans l'inhibition du vieillissement ou sénescence des cellules cutanées mammaliennes.

8. Dérivés de purine 6,9-disubstituée selon la revendication 2 pour utilisation dans l'inhibition du vieillissement ou sénescence des cellules cutanées mammaliennes.

9. Dérivés de purine 6,9-disubstituée selon la revendication 3 pour utilisation dans l'inhibition du vieillissement ou sénescence des cellules cutanées mammaliennes.

10. Dérivés de purine 6,9-disubstituée selon la formule générale I ou leurs sels pharmaceutiquement acceptables,



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dans laquelle R_6 est un groupe alkyle, alcényle, alcynyle, cycloalkyle, aryle, hétérocycle, hétérocycloalkyle, hétéroalkyle ou arylalkyle comprenant au moins un substituent hydroxyle et
dans laquelle R_9 est tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle ou 1-éthoxyethyle;
dans laquelle l'alkyle représente une chaîne alkyle ramifiée ou non ramifiée contenant 1 à 8 atomes de carbone pouvant, le cas échéant, être substituée indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes hydroxyle, halogène, alkyloxy, aryloxy, alkylamino, arylamino, amino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, alkyloxycarbonylamino, aryloxycarbonylamino, aryle, hétérocycle et hétéroaryle;
dans laquelle l'alcényle représente une chaîne alcényle ramifiée ou non ramifiée contenant 2 à 7 atomes de carbone avec au moins une liaison double, pouvant, le cas échéant, être substituée indépendamment par 1 à 6 substituants choisis parmi un groupe contenant de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino,

dans laquelle l'alcynyle représente une chaîne alcynyle ramifiée ou non ramifiée contenant 2 à 7 atomes de carbone avec au moins une liaison triple, pouvant, le cas échéant, être substituée indépendamment par 1 à 6 substituants choisis parmi un groupe constitué de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, alkyloxycarbonylamino et aryloxycarbonylamino ;
dans laquelle le cycloalkyle représente un groupe alkyle monocyclique ou polycyclique contenant 3 à 15 atomes de carbone pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino ;
dans laquelle l'aryle représente un groupe aromatique carbocyclique contenant 6 à 18 atomes de carbone avec au moins un cycle aromatique ou avec un cycle multiple condensé avec au moins un cycle aromatique lequel est substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino,
dans laquelle l'hétérocycle représente un groupe hétérocyclique contenant 4 à 9 atomes de carbone avec au moins un hétéroatome choisi parmi un groupe comprenant l'atome d'oxygène, de soufre et d'azote et pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino,
dans laquelle l'hétéroaryle représente un hétérocycle dans lequel au moins un cycle hétérocyclique est aromatique et pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino ;
dans laquelle l'hétérocycloalkyle représente un groupe -R_a-Het dans lequel Het est un groupe hétérocycle et R_a est un groupe alkyle pouvant, le cas échéant, être substitué indépendamment par 1 à 7 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino
dans laquelle l'hétéroarylalkyle représente un groupe -R_a-HetAr, dans lequel HetAr est un groupe hétéroaryle et R_a est défini ci-dessus ;
dans laquelle l'arylalkyle représente un groupe -R_b-Ar, dans lequel Ar est un groupe aryle et R_b est une chaîne de carbone ramifiée ou non ramifiée contenant 1 à 6 atomes de carbone et pouvant, le cas échéant, être substituée indépendamment par 1 à 5 substituants choisis parmi un groupe constitué de groupes alkyle, halogène, hydroxyle, alkyloxy, aryloxy, amino, alkylamino, arylamino, mercapto, carboxyle, cyano, nitro, carbamoyl, sulfo, sulfamido, acyle, acylamino, acyloxy, alkylthio, arylthio, cycloalkyle, aryloxycarbonylamino et alkyloxycarbonylamino ;
dans laquelle l'halogène représente un atome de fluor, brome, chlore ou iode,
dans laquelle hydroxy représente un groupe -OH,
dans laquelle mercapto représente un groupe -SH,
dans laquelle amino représente un groupe -NH_2,
dans laquelle carbamoyl représente un groupe -$CONH_2$,
dans laquelle cyano représente un groupe -CN,
dans laquelle carboxyle représente un groupe -COOH,
dans laquelle nitro représente un groupe -NO_2,
dans laquelle sulfo représente un groupe -SO_3R_c, dans lequel R_c est hydrogène ou alkyle,
dans laquelle sulfamido représente un groupe $SO_2NR_cR_c$', dans lequel R_c et R_c' sont indépendamment hydrogène ou alkyle,
dans laquelle acyle représente un groupe -$C(O)R_d$, dans lequel R_d est alkyle, aryle, arylalkyle ou cycloalkyle,
dans laquelle acyloxy représente un groupe -O-$C(O)R_e$, dans lequel R_e est alkyle, aryle ou hétérocycle,
dans laquelle acylamino représente un groupe -$NHCOR_f$, dans lequel R_f est alkyle, hétérocycle ou aryle,
dans laquelle alkyloxycarbonylamino représente un groupe -NHCOORg, dans lequel R_g est alkyle ou cycloalkyle,
dans laquelle aryloxycarbonylamino représente un groupe -$NHCOOR_h$, dans lequel R_h est aryle,
dans laquelle alkyloxy représente un groupe -OR_h, dans lequel R_h est alkyle, cycloalkyle ou arylalkyle,
dans laquelle aryloxy représente un groupe -OR_g, dans lequel R_g est aryle, dans laquelle alkylamino représente un groupe -NR_iR_j, dans lequel R_i est hydrogène, alkyle ou hétérocycle et R_j est alkyle ou hétérocycle,
dans laquelle arylamino représente un groupe -NR_kR_h, dans lequel R_k est hydrogène ou aryle et R_h est alkyle, aryle

ou hétérocycle,
dans laquelle alkylthio représente un groupe -SR_h, dans lequel R_h est défini ci-dessus, et
dans laquelle arylthio représente un groupe -SR_g, dans lequel R_g est défini ci-dessus,
destinés pour utilisation dans le traitement des maladies cutanées des mammifères.

11. Dérivés de purine 6,9-disubstituée selon la revendication 10, choisis parmi le groupe constitué de 6-(2-hydroxycyclopropylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxycyclobutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxycyclohexylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-chlorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-chlorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-chlorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-iodobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl) purine, 6-(4-hydroxy-5-iodobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-iodobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-bromobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-bromobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-bromobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-fluorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-fluorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-fluorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2,3-dihydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2,4-dihydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2,5-dihydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3,5-dihydroxy-4-chlorobenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-5-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl) purine, 6-(2-hydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyl, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-4-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-2-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3,5-diméthyl-4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3,5-dibrome-4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxyméthyl-3-méthylallyl)amino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(Z)-(4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(Z)-(1"-méthyl-4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(1'-méthyl-4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(1'-méthyl-4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-3-pyridylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-4-pyridylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(2-hydroxy-4-morpholinylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-hydroxy-1-pyrolidinylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-2-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-6-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(3-carboxy-4-hydroxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-2-méthoxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine et leurs sels pharmaceutiquement acceptables
destinés pour utilisation dans le traitement des maladies cutanées des mammifères.

12. Dérivés de purine 6,9-disubstituée selon la revendication 10, choisis parmi le groupe constitué de 6-(4-hydroxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxybenzylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(E)-(1'-méthyl-4-hydroxy-3-méthylbut-2-en-1-ylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(1'-méthyl-4-hydroxy-3-méthylbutylamino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthylanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine, 6-(4-hydroxy-3-méthoxyanilino)-9-(tétrahydropyran-2-yl, tétrahydrofuran-2-yl, 4-chlorobutyle, 1-éthoxyéthyl)purine et de leurs sels pharmaceutiquement acceptables destinés pour utilisation dans le traitement des maladies cutanées des mammifères.

13. Dérivés de purine 6,9-disubstituée selon la revendication 1 ou leurs sels pharmaceutiquement acceptables pour utilisation dans le traitement des réponses immunologiques résultant de, ou associées aux, inflammations cutanées mammaliennes.

14. Dérivés de purine 6,9-disubstituée selon la revendication 2 ou leurs sels pharmaceutiquement acceptables pour utilisation dans le traitement des réponses immunologiques résultant de, ou associées aux, inflammations cutanées mammaliennes.

15. Dérivés de purine 6,9-disubstituée selon la revendication 3 ou leurs sels pharmaceutiquement acceptables pour utilisation dans le traitement des réponses immunologiques résultant de, ou associées aux, inflammations cutanées mammaliennes.

16. Dérivés de purine 6,9-disubstituée selon la revendication 1 ou leurs sels pharmaceutiquement acceptables pour utilisation dans l'amelioration des effets indésirables de vieillissement sur les cellules mammaliennes.

17. Dérivés de purine 6,9-disubstituée selon la revendication 2 ou leurs sels pharmaceutiquement acceptables pour utilisation dans l'amelioration des effets indésirables de vieillissement sur les cellules mammaliennes.

18. Dérivés de purine 6,9-disubstituée selon la revendication 3 ou leurs sels pharmaceutiquement acceptables pour utilisation dans l'amelioration des effets indésirables de vieillissement sur les cellules mammaliennes.

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